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BLEEDING IN HIATUS HERNIA*

By OTTO D. SAHLER, M.D., *and* AUBREY O. HAMPTON, M.D.
BOSTON, MASSACHUSETTS

A STUDY of hiatus hernia, carried on at the Massachusetts General Hospital and covering a period of ten years, has brought out two important points, both of which merit greater emphasis than they have received in the past. One is that hemorrhage may be a symptom of hernia; the second, that the incidence of hiatus hernia is considerably higher than has been appreciated.

Richard Bright[1] in 1836 described a case of diaphragmatic hernia with ulceration. This is probably the earliest reported case of the kind. The earliest roentgenological report with a history of bleeding is that of Carman and Fineman[7] in 1924. One of their patients had a chronic anemia, while another vomited blood; a third vomited blood at least three times following an injury which led to a diaphragmatic hernia. The authors, however, did not correlate the blood loss in any of the 3 cases with the herniation.

In an excellent article in which he discusses the etiology of hernia, Åkerlund[1] presents 24 cases of his own and reviews 60 cases from the literature. Öhnell[17] in a second part of this paper points out the fact that 2 or 3 of their cases vomited blood, or had obvious bleeding on instrumental examination. This is the first correlation between hiatus hernia and bleeding which we found.

Bock[4] in a discussion of one of the Cabot case reports in 1929 was the first American to emphasize the presence of gastrointestinal tract hemorrhage with hiatus hernia. He cited 3 cases with occult blood in the stools and a secondary anemia in which the only roentgenological findings were those of hiatus hernia. In the same year Harrington[10] reported 30 cases of hiatus hernia operated upon, 8 of which had a definite history of bleeding from the gastrointestinal tract without any other apparent cause. Seven of these 8 cases were found at operation to have either erosion or ulceration of the mucosa in the herniated portion of the stomach. These 7 cases were found to be somewhat incarcerated.

Mathews and MacFee[14] presented 2 cases of proved ulcer in patients with diaphragmatic hernia, 1 of whom vomited blood late in the course of disease. They point out the fact that hiatus hernia may be the cause of anemia, especially if the stool is positive in the guaiac test. Truesdale[19,20] in 1932 was able to find only 17 cases of proved ulceration in diaphragmatic hernia. Weitzen[21] in the same year presented 2 cases of diaphragmatic hernia

* From the Department of Radiology, Massachusetts General Hospital, Boston. Presented at the Forty-first Annual Meeting, American Roentgen Ray Society, Boston, Mass., Oct. 1–4, 1940.

with bleeding, in 1 of which there was an apparent thickening and hypertrophy of the gastric rugae localized to the herniated portion of the stomach.

Bock, Dulin and Brooke[5] in 1933 presented 10 cases of diaphragmatic hernia with secondary anemia. Two came to autopsy. The gastric mucosa in the herniated portion was found to show large submucosal blood vessels with pin-point areas of hemorrhage, while that in the non-herniated portion appeared normal.

Gardner[9] presented 28 cases of diaphragmatic hernia with secondary anemia. Of these, 5 had true peptic ulcer, and in 8 the anemia was considered to be due to hernia. Gardner attributed the bleeding to venous congestion in the herniated portion of the stomach as a result of the muscular compression of the diaphragm. He advised first treatment for the secondary anemia in addition to a medical ulcer regimen, and if this proved unsuccessful, operation later.

Jones,[13] in an excellent paper on the clinical symptoms of hiatus hernia, mentions that in 91 cases of hernia, 4 cm. or less in size but in patients with definite symptoms of hernia, 22 had a history of bleeding. He found 6 cases of bleeding in 37 similar cases with larger herniae.

Morrison[16] and Healy[11] were the first to emphasize the relative frequency of non-traumatic herniae of the stomach through the esophageal hiatus. In 1925 Healy[11] stated that roentgenological study was the best method of diagnosing hiatus hernia. Schatzki[18] stressed the high incidence of hernia, especially in older patients. He found that in a group of 30 patients, sixty-five years of age or older, 14 had demonstrable hiatus herniae. By increasing the intra-abdominal pressure with air insufflation of the colon, he was able to show similar herniae in 8 additional patients. In other words, 73 per cent of a group of 30 elderly patients were found to have demonstrable hiatus herniae.

In order to determine the incidence of hiatus herniae in a group of clinic patients, one of the authors recently examined 100 consecutive patients during a two month period. Each patient was examined in both the upright and the horizontal positions with the esophagus filled with barium, and in both the left and right oblique position. In all cases manual compression of the epigastrium was used. Nine patients, 6 female and 3 male, showed a hernia. The average age of the entire group was 43.5 years while the average age of the 9 patients with hernia was 45.3 years, or slightly above that of the entire group. Most of the 100 patients were examined primarily for peptic ulcer and were in a fairly young age group, and it is our belief that the incidence of hernia would be even higher in an older age group. Even so, an incidence of 9 per cent is higher than that reported in a recent paper by Beilin,[2] and other authors, but it must be remembered that these cases were examined with special emphasis on hiatus hernia while the reports of other authors are taken from their general statistics, that is, they may not have looked especially for hiatus hernia.

Of the 9 patients with hernia in this small series, 3 gave a history of having vomited small amounts of blood, and 1 of the 3 showed roentgen evidence of gastritis on examination.

The incidence of hiatus hernia in a large clinic cannot be determined accurately unless the routine roentgen examination is directed toward this diagnosis; that is, unless each patient is examined in the horizontal position with the esophagus filled with barium. Some roentgenologists, notably Carty,[8] believe that herniae can be demonstrated in the upright position. Carty examines the patient in the upright right anterior oblique position at full inspiration and with pressure on the abdomen. In this position the barium will take an upward course as it enters the stomach, and in some cases only a "flip" of the barium column may be seen. While many herniae may be seen in the upright position we have found that they are better demonstrated in the horizontal position, and also

that many smaller herniae which are missed in the upright position become visible when the horizontal position is used. In the upright position the hernia empties rapidly and is drawn out into a shape similar to the lower end of the esophagus, so that the cardiac sphincter may not be seen and the asymmetrical relationship of the esophagus to the herniated fundus does not occur (Fig. 1 and 2).

Schatzki's proof that increased intra-abdominal pressure makes possible visualization of hernia previously unseen is additional confirmation, we believe, of our contention that the horizontal position is preferable to the upright position, because changes in intra-abdominal pressure occur in shifting from the horizontal to the upright position.

Jenkinson[12] in 28 cases of hernia found only 2 which were suspected of having hernia when examined in the upright position. In 1930, Moore and Kirklin[15] found that in 2 out of 32 selected cases which were called negative on examination in the upright position herniae were demonstrable in the prone position. Åkerlund[1] points out that the lesions are most often recognized with the patient in the prone or supine position, or lying on his right side. He adds that at times it may be necessary to apply manual compression to the epigastrium in order to demonstrate the hernia, and this is also our belief.

Fig. 1. Posteroanterior and both oblique views. A tracing of the lower esophagus of a patient with a definite history of hiatus hernia, made from spot film taken in the upright position. Note in the right hand view that the hernia cannot be distinguished from dilatation of the lower esophagus.

Method of Examination and Diagnosis

At the Massachusetts General Hospital all patients are examined in the prone, the supine and the standing position; and, in our opinion, many hiatus herniae would not be demonstrated if the supine and prone examinations were not made. The Trendelenburg position is also of value.

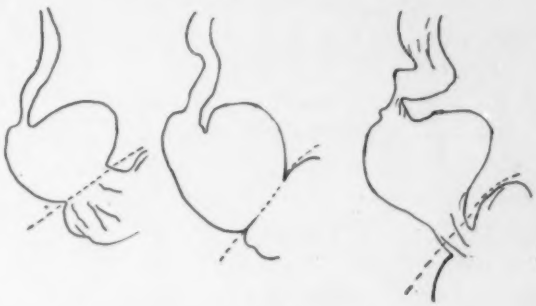

Fig. 2. Same as Figure 1. Notice in the horizontal position the increase in the size of the hernia. In all three views the hernia can be differentiated from esophageal dilatation.

When a patient is examined in the right anterior oblique position while supine and with the esophagus filled, the narrowing produced by the cardiac sphincter is seen above the herniated fundus. The constriction of the fundus is apparent as it passes through the diaphragm, as is the gastric mucosa. If the patient is turned to the left anterior oblique position the esophagus is seen to enter at the right anterior margin of the herniated fundus. This asymmetry of the relation of the esophagus with the collection of barium above the diaphragm is of considerable importance in establishing the diagnosis. The herniated portion also presents a dumbbell, or inverted molar tooth, shape* which is considered characteristic of hernia (Fig. 4). Care must be taken not to confuse dilatation of the lower end of the esophagus during peristalsis with a hiatus hernia, and if the facts just mentioned are kept in mind no confusion arises. It is not always possible to differentiate between the mucosal folds

* The term "inverted molar tooth shape" was first used by Dr. J. M. Robinson, now in the U. S. Navy.

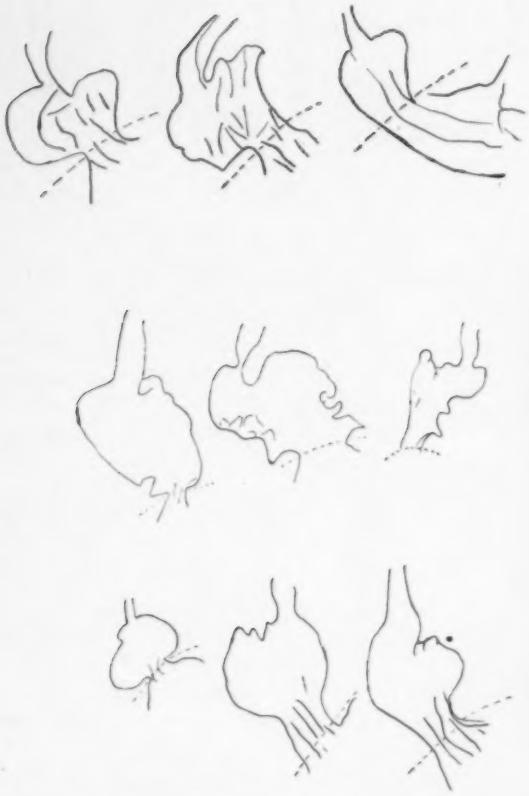

Fig. 3. Posteroanterior and both oblique views. Three different cases of hiatus hernia showing the relationship of the esophagus to the herniated fundus, and the relation of the diaphragm to the stomach.

Fig. 4. Left anterior oblique view. Note the asymmetrical relationship of the esophagus to the herniated fundus, the narrowing of the fundus as it passes through the diaphragm. This is a typical inverted molar tooth shape.

of the esophagus and the herniated fundus of the stomach, and at times it is difficult to localize the cardiac sphincter. In a rare case, the actual hernial sac may be seen in the lower mediastinum as a soft tissue mass, fusiform in shape and smooth in outline. The usual differential diagnosis

Fig. 5. A patient with a large hiatus hernia and a definite ulcer in the herniated portion of the stomach. Note the large ulcer in the herniated fundus and the soft tissue mass in the lower chest, due to the hernial sac. The presence of a soft tissue mass in this position should suggest the presence of a hiatus hernia.

of such a mass lies between metastatic or primary tumor and abscess; and the fact that hiatus hernia may cause a similar shadow is important. The diagnosis can be confirmed easily by a swallow of barium (Fig. 5).

STATISTICAL DATA

Between 1930 and 1940, 221 cases of hiatus hernia were reported in the Department of Radiology of the Massachusetts

General Hospital. This figure does not represent the total number of patients with hiatus hernia who had studies of the upper gastrointestinal tract, for in many cases the herniae were not recorded because the hernia were found in a period of less than two months. When one further considers that this series was compiled by one of the three regular roentgenoscopists in one division of the hospital it becomes evident that

TABLE I

GROUP I—PATIENTS WITH POSITIVE HISTORY OF UPPER GASTROINTESTINAL TRACT BLEEDING

Case	Age	Sex		Size Hernia	Hemoglobin Per Cent	Erythrocyte Count	Other Findings
		M	F				
K.C.	62		x	⅓ stomach	65	3.68	Hernial opening small, but emptied readily
M.K.	47		x	Small	?	?	None
I.C.	38	x		Small	70	4.1	None
J.O.	43	x		Large	51	3.55	Localized gastritis in herniated portion. No ulceration
E.O.	55		x	Small	?	?	Traction diverticulum of the esophagus
W.M.	65	x		6×4 cm.	90	5.2	Duodenal diverticulum. Sulfapyridine for pneumonia
W.R.	69	x		Small	65	4.5	Healing ulcer in upper body of stomach by gastroscopy
W.D.	69	x		Small	65	2.25	Questionable gastritis while bleeding
A.H.	46		x	6 cm.	75	5.34	Small diverticulum of second portion of duodenum
A.B.	63		x	Entire fundus	70	3.81	Hernia did not reduce
A.M.	68		x	5 cm.	70	3.85	Questionable ulcer in hernia by roentgen examination. Inflammatory stenosis of esophagus by gastroscopy
M.W.	55		x	4 cm.	42	1.23	Redness of mucosa around cardia by gastroscopy
M.P.	71		x	8 cm.	?	?	Diverticula of colon and esophagus. Given sulfapyridine. Ulcer in herniated portion at postmortem
C.M.	53	x		4 cm.	60	2.5	Gastritis in hernia by roentgen examination and gastroscopy
E.G.	71		x	2 in.	70	3.96	None
A.P.	50		x	¼ stomach	55	3.5	Swelling of folds in prepyloric area. Gastritis?
M.H.	50		x	Small	85	3.85	Gastritis on upper greater curvature with bleeding by gastroscopy
A.M.	60	x		Small	80	4.5	Hypertrophic gastritis high on posterior wall by gastroscopy
T.G.	55	x		Large	75	3.4	None
Total	19	8	11				

examiner did not always regard them of sufficient significance in the particular case under question.

As further evidence that these 221 cases are not the exact number seen in a period of ten years is the fact that in 100 patients examined by one of the authors, 9 cases of the total of 221 reported cases in ten years is far too small a figure.

An analysis was made of the 221 cases with special attention given to the incidence of bleeding. This group included patients whose hernia was associated with cancer or ulcer of the stomach; but, where

TABLE II

GROUP 2—PATIENTS WITH POSITIVE HISTORY OF GASTROINTESTINAL TRACT BLEEDING WITHOUT HEMATEMESIS

Case	Age	Sex		Size Hernia	Hemoglobin Per cent	Erythrocyte Count	Other Findings
		M	F				
E.L.	53		x	4 cm.	65	3.77	Gastritis in hernia. Diverticula of colon and duodenum
H.C.	62	x		Small	8 gram	2.92	Sigmoid diverticula
N.C.	82	x		?	60	2.9	Question of polyps on barium enema
J.v.M.	60	x		Large	38	2.9	None
J.F.	64		x	½ stomach	5 gram	3.9	None
H.U.	66		x	Moderate	50	2.96	None
C.B.	50		x	3 cm.	80	4.0	Question of duodenal ulcer
J.L.	74	x		Small	70	3.47	None
C.M.	63	x		½ stomach	58	3.9	Large ulcer in herniated portion of stomach. This decreased in size with treatment
Total	9	5	4				

such obvious cause for bleeding existed, they were excluded from the number whose hemorrhage was considered as due to hernia. On the other hand, cases of hernia with other gastrointestinal tract pathology, such as diverticula, a rather infrequent cause of hemorrhage, are included in the group with bleeding due to hernia. Our material for study can be divided into three broad groups:

1. Patients with a positive history of hematemesis. This group contains only those with relatively high gastrointestinal tract hemorrhage, and is by far the most important (Table I).

2. The remaining patients with gastrointestinal tract hemorrhage, without hematemesis. Included in this group are all those with tarry stools and guaiac positive stools. Bleeding in a certain number of these is probably due to polyp or other pathology which was not diagnosed despite repeated barium enemas (Table II).

3. Patients exhibiting anemia of some severity without a positive history of gastrointestinal tract bleeding and in whom no other cause for amenia except hernia was recognized (Table III).

Nineteen patients fell into Group 1; 11 females and 8 males (Table I). The ages of the patients range between thirty-eight and seventy-one years, with an average age of fifty-seven years. The roentgen report gives the size of the hernia as "small" in 7 pa-

TABLE III

GROUP 3—PATIENTS WITH NO HISTORY OF GASTROINTESTINAL BLEEDING

Case	Age	Sex		Size Hernia	Hemoglobin Per cent	Erythrocyte Count	Other Findings
		M	F				
E.A.	75		x	½ stomach	60	3.62	None
E.M.	67		x	Moderate	65	3.22	Vomiting without blood
I.T.	62		x	Entire fundus	50	2.2	Esophageal diverticulum
S.P.	69		x	¾ stomach	45	3.5	Did not reduce in upright position
Total	4		4				

tients; as "at least 4 cm. in diameter" in 7, while the actual measurement of the hernia is not noted in 5. It was, however, apparently large in this last 5, the size being from one-quarter of the stomach to the entire fundus.

In 10 of the 19 cases there was evidence of either gastritis or ulceration, as determined by roentgenography, gastroscopy or postmortem examination. It is hard to gather from the gastroscopic report wheth-

Fig. 6. Spot film of Figure 5 showing the ulcer crater.

er the ulceration and gastritis were actually in the herniated portion of the stomach, but where a definite location is given it is always high in the stomach in a position where the hernia would exist. One patient developed pneumonia while in the hospital. She was given sulfapyridine, and subsequently developed hematemesis. Postmortem examination of this patient showed the upper 8 cm. of the stomach to lie in a herniated sac, and an ulcer, measuring 1.5 by

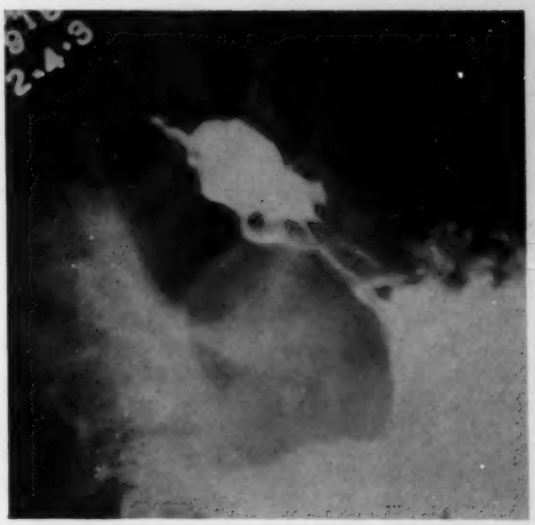

Fig. 7. Patient C. M. (Table II). Note the large pool of barium above the diaphragm. This represented the actual ulcer crater.

0.5 long by 1 mm. deep, was found on the anterior wall 4 cm. from the cardiac orifice.

Two of the patients had esophageal diverticula, and in 3 there were duodenal diverticula. One patient showed an inflammatory stenosis of the esophagus by esophagoscopy and a questionable ulcer in the hernia by roentgenography. In 4 patients hernia was the only gastrointestinal tract

Fig. 8. Spot film of the ulcer crater in Figure 7.

pathology noted. We believe the frequent incidence of gastritis and ulceration high on the stomach wall to be very significant (see Fig. 5, 6, 7 and 8).

In Group 2 (Table II) there are 5 male and 4 female patients, whose ages vary from fifty to eighty-two years, with an average age of sixty-four years. In 2 patients, the size of the hernia was small; in 5, it varied from 3 cm. in diameter to half the size of the stomach; in 1, the size is not noted. Patient E.L. showed a definite gastritis in the herniated portion of the stomach roentgenologically. Patient C. M. had a large ulcer in the herniated portion of the stomach, which responded well to dietary treatment (Fig. 7 and 8). Patient N.C. showed questionable polyp of the colon, and patient C.B. questionable ulcer in the duodenum. Patient H.C. had, in addition to the hernia, diverticula of the sigmoid. Four patients in Group 2 showed hiatus hernia only.

Group 3 (Table III) was made up of 4 females. The hernia in all 4 was fairly large. One patient had a history of vomiting, but the vomitus at no time was seen to contain blood. Patient I. T., who had a very poor dietary history, had a diverticulum of the esophagus. The fourth patient had diverticulitis seven years after the hiatus hernia was found.

DISCUSSION

In a series of 221 cases of hiatus hernia, 32 had either moderately marked anemia or a positive history of gastrointestinal tract bleeding. We believe that the high incidence of gastrointestinal tract bleeding associated with hiatus hernia is evidence that the hernia may produce bleeding. In several cases active bleeding was noted at the gastroscopic examination. We obviously have no proof that all of the 32 cases actually bled in the herniated fundus and we do not mean to convey the impression that the incidence of bleeding from hiatus hernia is 15 per cent, as might be assumed from our data. Bleeding when present (particularly hematemesis) may be due to the hernia, and it may be produced by congestion of the blood vessels in the herniated portion of the stomach with a resultant change in the mucosa, and gastritis or ulceration. This theory is borne out by the fact that 10 of 19 cases with hematemesis showed changes in the upper stomach—changes proved by roentgen, gastroscopic or postmortem examination. We believe also that there is always some mucosal disturbance in cases of hiatus hernia which bleed. Benedict[3] has stated that the cases of hiatus hernia with bleeding which he has observed gastroscopically have shown gastritis and that he considers the bleeding due to the gastritis.

In those cases where there was no positive history of bleeding the anemia may be explained on a dietary basis, or there may have been slight blood loss which was not detected.

SUMMARY AND CONCLUSIONS

1. The diagnosis of hiatus hernia is dependent on two roentgenologic points: one, an asymmetrical relationship between the lower end of the esophagus and the herniated fundus of the stomach; and the other a narrowing of the fundus where it passes through the diaphragm.

2. A soft tissue mass in the lower mediastinum should suggest the possibility of hiatus hernia as well as the usual differential diagnosis of tumor or abscess.

3. The incidence of hiatus hernia is much higher than is generally recognized.

4. Hiatus hernia may be the cause of bleeding.

5. Bleeding caused by hiatus hernia is probably due to constriction of the hernial ring with resultant gastritis and ulceration of the herniated fundus. If neither gastritis nor ulceration is present the lesion will not cause bleeding.

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BLEEDING ASSOCIATED WITH EXTRAMUCOSAL TUMORS OF THE STOMACH*

By OTTO D. SAHLER, M.D., *and* AUBREY O. HAMPTON, M.D.
BOSTON, MASSACHUSETTS

THE purpose of this paper is to point out the relatively frequent occurrence of gastrointestinal tract bleeding in the presence of intramural submucosal tumors of the stomach, and to emphasize their differential diagnosis.

The term "extramucosal tumors of the stomach" is a very broad, all-encompassing one, including a large variety of histopathologically different tumors. Among the extramucosal tumors of the stomach are leiomyoma, leiomyosarcoma, fibroma, fibrosarcoma, neuroma, neurosarcoma, lymphoma, hemangioma, lymphangioma and aberrant pancreatic tissue. In the present discussion we are primarily interested in the tumors of nerve, muscle and fibrous tissue origin, in both their benign and malignant forms.

REVIEW OF LITERATURE

Campbell[2] in 1915 collected 40 cases of benign tumors of the stomach, most of which proved to show areas of either fibrosarcomatous or myosarcomatous degeneration. He states that fibromata may show a punched-out ulcer. Basch[1] credits Morgagni with having described in 1762 the first myoma of the stomach. In 1919 Holmes[3] described 3 cases of pedunculated tumor of the stomach. Two of these cases were fibrosarcoma and are included in the present report. The third case was a lymphangio-endothelioma, and is not included in the present series. Holmes emphasized the fact that in these cases the peristaltic waves passed over the involved area of the stomach without evidence of break such as is seen in lesions which involve the gastric wall.

Moore,[5] in an excellent paper, discusses in some detail the roentgenological diagnosis of benign tumors of the stomach. He states: (1) Benign tumors produce a filling defect which is circumscribed and punched out in appearance. (2) The filling defect is usually on the gastric wall leaving the curvature regular and pliant. (3) While the rugae are obliterated in the immediate area of the tumor, as in inflammatory and malignant lesions, the rugae surrounding a benign tumor are more nearly normal in their arrangement and distribution. (4) They cause little or no disturbance in peristalsis and retention is uncommon except when the lesion is at or very near the pylorus. (5) They do not reveal a niche, nor is there any incisura or other evidence of spasm. (6) They are rarely sufficiently large to be palpated.

Minnes and Geschickter[4] in a review of the literature were able to collect 341 cases of leiomyoma, 102 cases of neurofibroma, 42 cases of fibroma, 32 cases of lipoma, 1 osteoma, 1 osteochondroma, 3 myomata, and 3 pancreatic arrests in the stomach. In addition, they presented 50 cases of their own.

Odqvist[6] described a case of a gastric neurinoma in which the chief clinical sign was hemorrhage. Roentgen examination of the patient showed the presence of a well circumscribed tumor of a benign type with a stamped out niche. Odqvist believes that the niche formation in gastric neurinoma is generally produced by necrosis and loss of a central area of the tumor into the lumen of the stomach.

Senturia[8] emphasizes that hemorrhage is a common clinical finding in gastric neurinoma. He reports a case with an oval to round, smoothly outlined defect with an "en face niche."

The roentgenological diagnosis of these

* From the Department of Radiology, Massachusetts General Hospital, Boston. Presented at the Forty-first Annual Meeting, American Roentgen Ray Society, Boston, Mass., Oct. 1–4, 1940.

extramucosal intramural tumors of the stomach is dependent on the presence of a space-occupying, smooth or lobulated, partially pedunculated, usually sessile mass projecting into the lumen of the the stomach from its wall (Fig. 1). The tumor, if viewed in profile, appears as extrinsic but is freely movable with the stomach. The mucosal pattern of the stomach as a whole is normal. The mucosa adjacent to the tumor is pliable.

The mucosa over the tumor appears smooth and without its normal folds (Fig. 3, *A* and *B*). In contrast to an extrinsic pressure defect the defect produced by the tumor forms a definite abrupt angle with the uninvolved wall of the stomach. This angle is usually obtuse but may be acute. In the rare cases in which the tumor protrudes like a polyp into the gastric lumen an acute angle is seen.[7] If viewed en face the barium shadow at the obtuse margin fades out gradually; that is, the tumor is not sharply defined, but at other points the tumor edge may be quite sharp. The pseudopedunculated appearance of part of the margins is probably due to traction on the gastric wall (Fig. 1). An ulcer may or may not be present, but when present is helpful in making the diagnosis (Fig. 4). Such an ulcer is usually deep and smooth, the depth as a rule being as great as the width (Fig. 5, *A* and *B*). There is, however, no tendency toward spasm or incisura on the opposite gastric wall The ulceration in carcinoma and the pseudo-ulceration in pancreatic arrests are nearly always in the center of the lesion, in contrast to the irregularly placed ulcerations of intramural tumors.

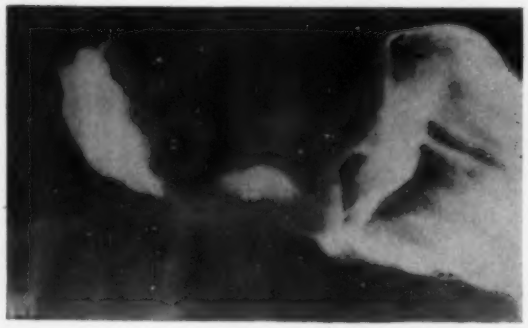

Fig. 1. Note the obtuse angle between stomach and tumor (arrow). There is a smooth defect as if a mass were pressing in from the outside.

Fig. 2. There is a large space-occupying mass in the stomach. Note that it is coarsely lobulated and that there is relatively normal mucosa above and below the tumor with smooth mucosa in the region of the tumor.

Roentgenologically these tumors must be differentiated from cancer and benign polyps. They can usually be differentiated from cancer by the relative normality of the adjacent mucosa. Other differential guides are the sharpness and the smoothness of outline, and the angle formed at the gastric wall junction. At times, however, it is impossible to differentiate the two types of tumor as was shown in a recent case which roentgenologically was diagnosed as either carcinoma or lymphoma, but which proved to be a necrotic, widely ulcerated fibrosarcoma (Fig. 6, *A* and *B*).

The most common finding which distinguishes these tumors from polyps is that they are usually sessile, whereas polyps are often pedunculated. An additional diagnostic point is the presence of ulceration of the deep type and the relatively smooth

contour of these tumors contrasted with the more lobulated appearance of polyps.

Occasionally a pancreatic arrest in the stomach makes absolute differential dinosis impossible, since these arrests lie in the gastric wall, and the duct opening from the arrest may closely simulate the ulceration of an intramucosal tumor. Pancreatic arrests, however, do not bleed, so the presence of bleeding would favor the diagnosis of other submucosal tumors (Fig. 7).

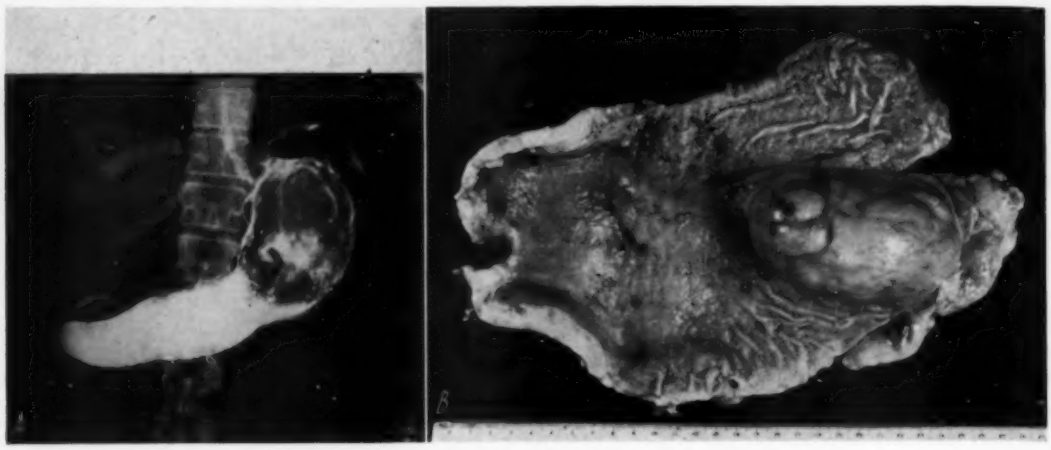

Fig. 3. Case xxii. *A*, leiomyoma. Note the broad attachment at the lesser curvature and the smooth surface of the tumor. *B*, photograph of the tumor. The mucosa over the tumor is smooth. There is hypertrophy of the antrum.

Gastroscopy is of value in diagnosing submucosal tumors, but its value is dependent upon the ability of the gastroscopist. In our own experience the gastroscopist missed the lesion entirely in his first case, while in the last he diagnosed it correctly in the face of a contrary roentgen diagnosis.

The gastroscopic findings are those of a tumor covered by smooth, rather atrophic mucosa, which may show ulceration in one or possibly more areas. The ulceration is, however, relatively small in comparison with the total size of the tumor and the mucosa beyond the actual area of ulceration, but overlying the tumor, shows no evidence of infiltration.

In the past twenty-seven years 24 intramural tumors of the stomach have been removed surgically at the Massachusetts General Hospital.* Twenty-one of the 24 patients have had fairly adequate roentgen examinations.

A review of the available *clinical* data shows the following:

1. Seventeen patients had symptoms of gastric distress, varying from gas and eructation to true abdominal pain similar to ulcer pain, and even including a sensation of "a ball bouncing around in the stomach."

2. Twelve patients gave a positive history of vomiting.

3. Bleeding from the gastrointestinal tract was experienced by 16 patients. (There is one additional case of presumptive bleeding, the patient having been admitted to the hospital because of very severe anemia, the red blood count having dropped from 3,200,000 to 2,000,000 in three weeks. Though no definite statement on hematemesis or tarry stools is made, further confirmative evidence of such bleeding is found in the fact that the tumor showed marked ulceration, and that after operation the anemia, which had failed to respond to vigorous preoperative therapy, cleared promptly.) Of these 16 cases, 7 had a

* A number of these cases have been published in the *New England Journal of Medicine* as "Case Reports from the Massachusetts General Hospital."

history of hematemesis and 10 passed occult blood in the stool. One patient had a guaiac positive gastric analysis.

4. In 3 patients a definite mass was palpable in the epigastrium.

5. Weight loss was noted in 7 patients.

The following reports represent rather typical cases.

CASE REPORTS

Case XXII (Fig. 3, *A* and *B*). R. B., white female, aged fifty-four, was admitted to the hospital on May 21, 1940, with the chief complaint of weakness and gas on the stomach for ten weeks. She had a history of nausea and vomiting for twenty-four years associated with a smothering feeling in the epigastrium. For six months she had noted weakness, vertigo, and tarry stools. Ten weeks before admission she fainted while going to the bathroom. Following this she passed a large black stool which was guaiac positive. Roentgen examination at another hospital was said to show a gastric ulcer on the posterior wall.

On physical examination the patient was obviously anemic. The red count was 4,680,000 and hemoglobin was 55 per cent.

Roentgen examination showed a large oval, smooth, slightly lobulated mass in the body of the stomach, over and around which the barium passed before it entered the antrum of the stomach. The mass measured 12 by 8 by 8 cm. It was slightly movable and was attached to the lesser curvature by a broad base. The pedicle measured at least 5 cm. in width, the upper border being 1 inch inferior to the cardiac orifice.

The gastroscopic report is as follows: In the body of the stomach anterior to the gastroscope and somewhat below it as it lay against the posterior wall there was a rounded, slightly nodular mass covered by smooth, normal appearing mucosa. The entire tumor could not be well visualized, and although the area of the greater curvature was somewhat obscured by retained secretion the impression was that of a non-ulcerated tumor lying below the mucous membrane and presumably attached along the anterior wall and lesser curvature.

At operation the stomach contained a large, freely movable, firm to hard, irregular mass which appeared to measure about 6 by 4 inches. This was in the fundal portion of the stomach close up to the cardia. A total gastrectomy was done.

Fig. 4. Note the sharply punched-out ulcer in the tumor and the absence of mucosal infiltration above the tumor. (Courtesy of R. G. Vance, M.D.)

The pathological report is as follows: The specimen is a subtotally resected stomach measuring 12 cm. along the lesser curvature and 25 cm. along the greater curvature. The serosa is salmon-pink, smooth and glistening throughout. The wall of the pylorus is markedly thickened, apparently due to hypertrophy of the muscularis, which measures 1 cm. in thickness. The mucosa is bright pink with a few small dark red areas scattered throughout. The rugae are not prominent. There is no visible ulceration. Originating in the superior resected border and lying in the lumen of the stomach is a large, firm, pedunculated mass, measuring 10 by 7 by 6 cm. The overlying mucosa is not adherent, and the pedicle is small compared to the size of the mass. On section it is firm, and the cut surface presents a grayish-yellow appearance with numerous irregularly scattered dark red, apparently hemorrhagic areas. Histological examination showed the tumor to be a leiomyoma.

Case XXIII (Fig. 5, *A* and *B*). E. F. L., white female, aged fifty, was admitted to the hospital with the chief complaint of a massive hematemesis six weeks before admission. The patient had felt faint upon arising one morning and went to the bathroom, at which time she

vomited about 1 pint of blood. She had no recurrence of hematemesis but felt fatigued.

Roentgen examination showed a mass 7.5 by 7.5 cm. arising from a broad base on the lesser curvature and posterior wall of the fundus of the stomach. The base of the tumor lay just posterior to the cardia. The surface of the mass was rather smooth although there was slight lobulation present. One deep, crater-like depression was seen in the lateral portion of the mass. In changing from the horizontal to the upright position the mass showed only a slight shift in its position within the stomach. The remainder of the stomach presented no pathologic change. The findings were interpreted as those of a tumor in the area described with a deep ulceration. Although several features were a little unusual the roentgenoscopist considered a leiomyoma or a similar tumor as the most probable diagnosis, and carcinoma less likely.

The gastroscopic report was as follows: In the upper part of the body of the stomach in the five o'clock position there was a smooth, rounded submucosal tumor of an elongated shape, appearing to be approximately 5 by 7 cm. in width and elevated above the surrounding mucosa by about 1 to 1.5 cm. There was no visible break in the mucosa overlying this tumor. Near its base the rugae started to pass over the tumor but were gradually flattened out. The mucosa surrounding the lesion was markedly atrophic with blood vessels clearly visible shining through. The findings were those of benign submucosal tumor with atrophy of gastric mucosa. The tumor appeared to extend to within about 1 cm. of the cardia, but did not involve the cardia.

The patient was operated upon and a fundusectomy was done. The pathological report is as follows: The specimen is a segment of stomach measuring 10 by 7 cm. At one edge of the specimen is a round, firm, lobulated, red-pink smooth mass covered by mucosa and measuring 6.5 cm. in diameter. It projects 2.2 cm. above the mucosal surface of the stomach. The center of this mass contains a round, punched-out, gray-pink, irregular ulceration 1.6 cm. in diameter and 0.5 cm. in depth. Just proximal to this ulcer is a small round, punched-out similar depression 4 cm. in width. There is normal appearing gastric mucosa on either side of the mass measuring 4 cm. on one side and 5 cm. on the other. This intramucosal mass extends through the wall as an extrinsic soft, ovoid, lobulated, smooth surfaced, dark-red mass measuring 5.5 by 6.5 by 4.5 cm. On section this contains a cyst filled with old blood, measuring 3 cm. in diameter, surrounded by a soft, necrotic, gray-red rim of tissue measuring up to 1 cm. in thickness. The tumor is slowly growing but has a fair number of mitoses. It is a neurogenic fibrosarcoma.

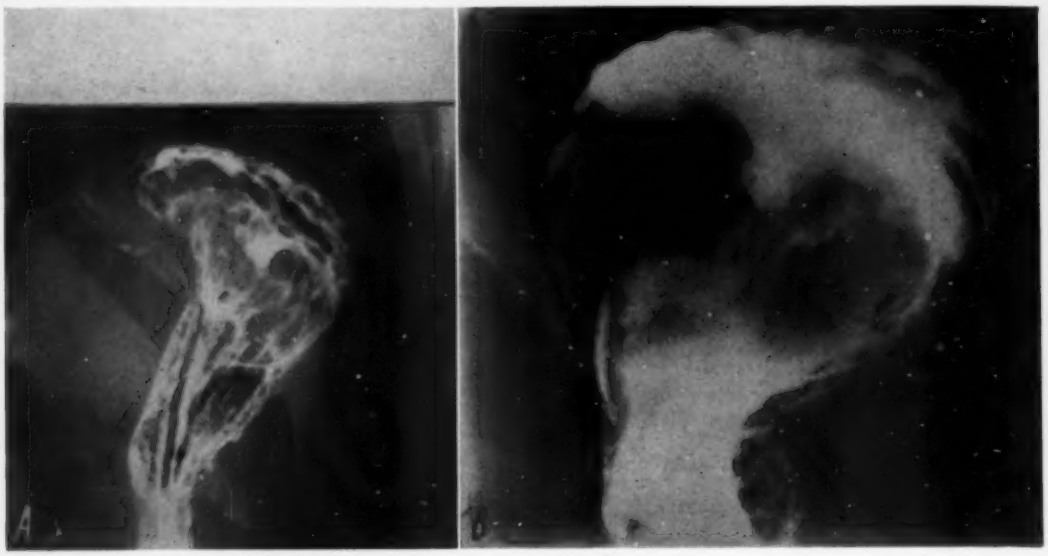

Fig. 5. Case xxiii. *A*, leiomyosarcoma. Note the ulcer which is as deep as it is broad. *B*, spot film of ulcer.

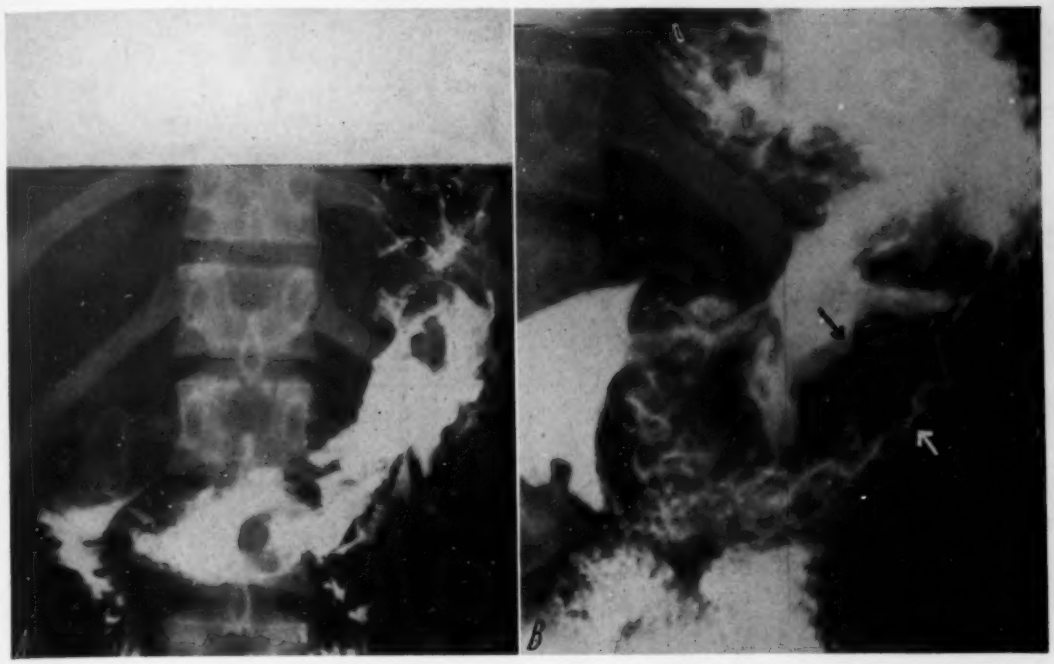

Fig. 6. *A*, a fibrosarcoma with the appearance of a carcinoma. Note the apparent mucosal infiltration and the large irregular ulcer crater. *B*, the margin of the irregular ulceration is unusually broad (arrows). Note the relative absence of normal mucosa and the ragged ulcer crater. This case was roentgenologically classified as a carcinoma. Gastroscopically, the tumor was thought to be extramucosal.

ROENTGEN FINDINGS

In some of the cases the roentgen reports are very brief, while in others fairly full descriptions of the findings are given. Of the 21 cases adequately examined roentgenologically, 20 showed a definite filling defect, which was described as "round" in 7 cases, "smooth" in 9, and "lobulated" in 3. The examiner noted that the outline was "sharp" in 4 instances, and in 9 intraluminal projection was definitely noted. Nine cases showed ulceration. In 1 patient the tumor was not found roentgenologically, despite repeated review of the films pre- and postoperatively. At operation for cholecystitis a small tumor was palpated in the region of the fundus and removed.

Two cases of ectopic pancreas were also seen. Both of thsese showed a definite smooth defect in the stomach, the defect being rounded but in the center there was a smooth dimple. In neither case was there the history of bleeding one would expect, since the dimple did not represent an ulcer crater but the lumen of the duct for the aberrant pancreatic tissue.

An analysis of the position of the lesion showed:

	Cases
Anterior wall	4
Posterior wall	6
Lesser curvature	8
Greater curvature	5
Not stated	1
Upper third stomach	7
Middle third stomach	6
Lower third stomach	11

CLINICAL FINDINGS

Of a total of 24 cases of intramural submucosal tumors of the stomach 16 had a positive history of gastrointestinal tract bleeding and 1 additional case had a presumptive diagnosis of bleeding. One other case in which "questionably tarry stools" is noted, was not included in this group. It becomes apparent that gastrointestinal bleeding is one of the most common symptoms in these cases since it occurred in 66.6 per cent of the patients. The only clin-

Fig. 7. Aberrant pancreas. Note the intramural defect. Arrow indicates the dimple at the site of the duct.

ical symptom of greater frequency was epigastric distress, but as this distress varied so greatly from patient to patient, from mere "gas" or "belching" to "severe pain" bleeding must be considered the most constant symptom. Bleeding is all the more significant when one considers that in 2 of the cases bleeding was mentioned as the only symptom. Analysis of the type of bleeding shows that in 7 there was definite hematemesis; in 1, the gastric contents was guaiac positive; and in 10, the stools were either markedly tarry or guaiac positive. In several of the patients there was a combination of these signs.

PATHOLOGICAL FINDINGS

Of the 16 cases with a history of bleeding, pathological examination of the surgical specimen showed 9 with definite ulceration in the tumor; 5 with no ulceration; and in 2, ulceration is not mentioned.

Of the 8 cases in which there appeared to have been no bleeding, 1 showed ulceration and 7 showed no ulceration. The pathological diagnoses in the entire group of 24 cases* were:

	Cases
Leiomyoma	8
Leiomyosarcoma	6
Neurofibrosarcoma	4
Neurofibroma	2
Sarcoma	2
Fibrosarcoma	2
Fibroma	1

PROGNOSIS

Of the 24 cases which were operated upon 2 died immediately postoperatively, 1 having had a severe anemia, and the other developing sepsis.

In 3 patients the tumor recurred; 1, a neurofibrosarcoma, with recurrence after six years, died of peritonitis after an operation for recurrence; 1, a sarcoma, recurred after four years; and the third, a fibrosarcoma, recurred after two and a half years.

The follow-up of these patients is not complete, but it is known that 1 patient lived for twenty-five years, 1, for nine years, 1 for seven years, and 6 for at least two years. Five patients have been operated on within the last two years. One patient died of intercurrent disease; 4 cannot be traced.

SUMMARY AND CONCLUSIONS

1. A smooth mass, round or ovoid, usually sessile, in the wall of the stomach should suggest an extramucosal tumor. When viewed in profile, at first glance these tumors may appear to be extrinsic, but in contrast to extrinsic pressure defects the uninvolved wall of the stomach forms an abrupt angle with the tumor defect. This angle may or may not be obtuse, but it is acute only in the rare cases in which the tumor protrudes like a sessile polyp into the stomach. The filling defect moves with the stomach and there is very little alteration in peristalsis.

2. Ulceration, which is relatively deep,

* One case had two different types of tumor.

smooth, and small in comparison with the size of the tumor, is common and should suggest the diagnosis.

3. Bleeding is the most common, constant symptom in extramucosal tumors of the stomach.

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SECONDARY LYMPHOSARCOMA OF THE STOMACH

By FRANZ BUSCHKE, M.D., *and* SIMEON T. CANTRIL, M.D.
From the Tumor Institute of the Swedish Hospital
SEATTLE, WASHINGTON

IT IS the purpose of this report to call attention to a certain type of lymphosarcoma of the stomach secondary to a known focus of lymphosarcoma in some distant part of the body outside of the abdominal lymphatic area and characterized by a roentgen appearance suggestive of a solitary malignant lesion of the stomach. This type of lesion is probably more common than is generally recognized.

The most common site of primary localized lymphosarcoma is the lymphoid tissue of the pharynx, stomach, ileum and cecum, and possibly in some lymph nodes themselves. It is a well known fact that secondary deposits from lymphosarcomas of the pharynx in their late stages tend to involve the abdominal lymph nodes. With the clinical picture of a general abdominal distress, the palpatory findings of abdominal masses and the knowledge of a previously treated lymphosarcoma in the pharynx, one may easily overlook the lesion in the stomach itself if roentgen examination of the stomach is not performed as a routine procedure. One may argue that this omission is of little significance since these cases are hopeless anyway. Their occasional importance, however, lies in the possibility of taking such a solitary malignant lesion seen in the roentgenogram for a primary carcinoma or a primary lymphosarcoma of the stomach if the primary lesion has been treated some time ago and the new examiner is not informed as to the previous presence of such a lesion or if the primary lesion has been overlooked. After successful treatment of a lymphosarcoma of the pharynx no trace of tumor or lymph nodes will be found in this original focus of the disease. The assumption of a primary lymphosarcoma of the stomach in such a case would render a slightly more hopeful prognosis since definite cases of primary lymphosarcoma of the stomach cured by irradiation or surgery are on record (Taylor[4]). Furthermore it seems that occasionally even in cases of a secondary lymphosarcoma of the stomach a cure or long intervals of good health may be obtained by radiation therapy. This seems to be a possible interpretation of the case reported by Schindler which will be reviewed presently. It seems, therefore, that the knowledge of this clinical picture which forms a fairly characteristic entity is not entirely of academic pathologic interest.

Case 1. Our own case observed here recently was that of a white male patient, O. M. S., aged fifty-seven. This patient was admitted on May 29, 1940. Seven weeks prior to that time he noticed the sensation of a foreign body in the roof of the mouth and shortly afterward a lump under the right jaw. Three weeks prior to admission he consulted his local physician who took a biopsy which showed lymphosarcoma. On admission here we found a large necrotic tumor mass occupying the region of the right tonsil with a necrotic ulceration (Fig. 1) The tumor bulged across the midline of the nasopharynx and there was a nodular infiltration of the soft palate with ulceration. Nasopharynx and lateral nasopharyngeal wall were clear. There was a nodularity with ulceration on the posterior surface of the soft palate and a nodular extension of the tumor into the hypopharynx along the posterior pillar down to the level of the epiglottis. There was a lymph node 3 cm. in diameter under the right mandible anterior to the sternocleidomastoid muscle. This node was fairly firm and slightly tender. Anterior to this there was a smaller lymph node; both nodes were movable.

This patient received roentgen therapy from May 29 to July 6, 1940: 6,975 r (measured on the skin) in thirty-nine days with 800 kv. radiation to one right lateral field which included the right lateral nasopharynx, tonsil, hypopharynx and regional lymphatic area.

Through the main course of treatment this field measured 12 by 8 cm. to 10 by 8 cm. The tumor responded readily to radiation therapy and had considerably regressed on the seventh treatment day after 775 r. The lymph node had almost disappeared on the ninth day after 1,375 r. Thirteen days after the end of treatment the skin reaction had entirely healed, the patient was gaining weight, and there remained only a scar at the site of previous biopsy on the anterior pillar at the junction with soft palate as the only reminder of the previous lesion. No lymph nodes were palpable.

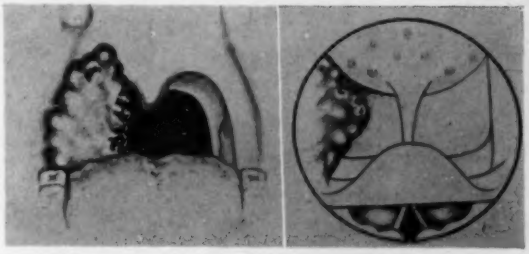

FIG. 1. Case 1. Lymphosarcoma of tonsil. Before treatment.

The following observation, however, showed that this patient did not continue gaining weight as we would anticipate in the case of a sterilized lesion. During the following months we searched repeatedly for metastatic foci in the chest and by clinical examination of palpable areas but did not find any indication of spread of the disease. In August, 1941, about one year after the end of treatment, the patient noticed a swelling of his legs up to the groin. The pharynx at this time appeared perfectly normal and there were no regional lymph nodes palpable. There was a small node 2 cm. in diameter in the left axilla. In the abdomen could be felt two masses of about 5 cm. in diameter each on the right and left side of the umbilicus. His complaints were very undetermined and only of a general abdominal distress. On the basis of the reports in the literature, which we will mention later, we examined the stomach roentgenoscopically and found a large ulceration on the greater curvature (Fig. 2*A*). We interpreted this as secondary lymphosarcoma of the stomach in view of the history of previous lymphosarcoma elsewhere. From the roentgen appearance alone I do not think that any diagnosis beyond that of a malignant ulceration of the stomach could be made or that this lesion could be differentiated from a carcinoma. On August 26, 1941, Dr. Ralph Loe did a gastroscopy and found on the greater curvature at the posterior wall an elevated lesion with a great central ulceration. This lesion was circumscribed and seemed to consist of multiple submucous

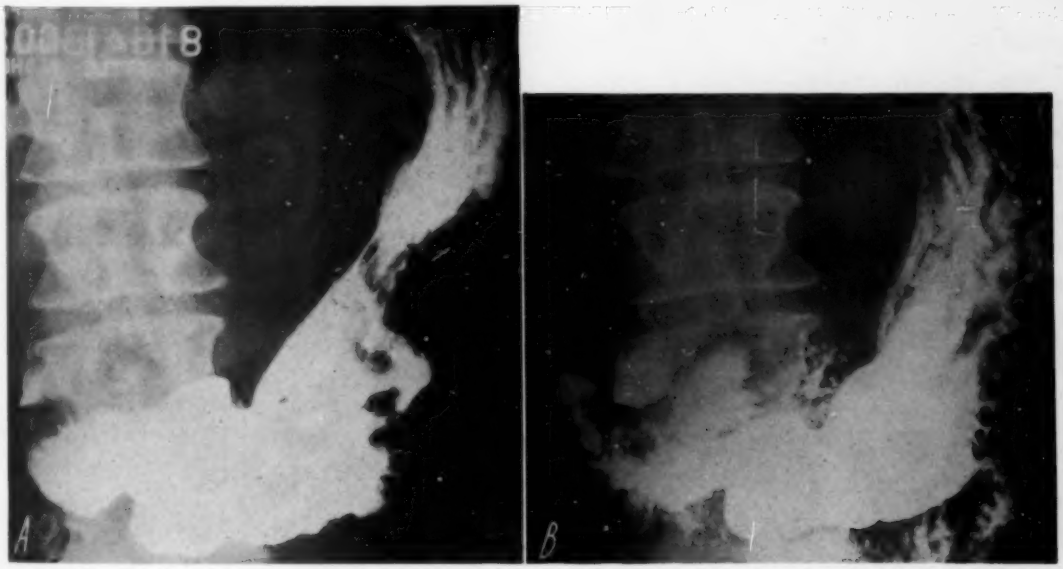

FIG. 2. Case 1. Secondary lymphosarcoma of stomach showing roentgen appearance. *A*, before treatment; *B*, after roentgen therapy.

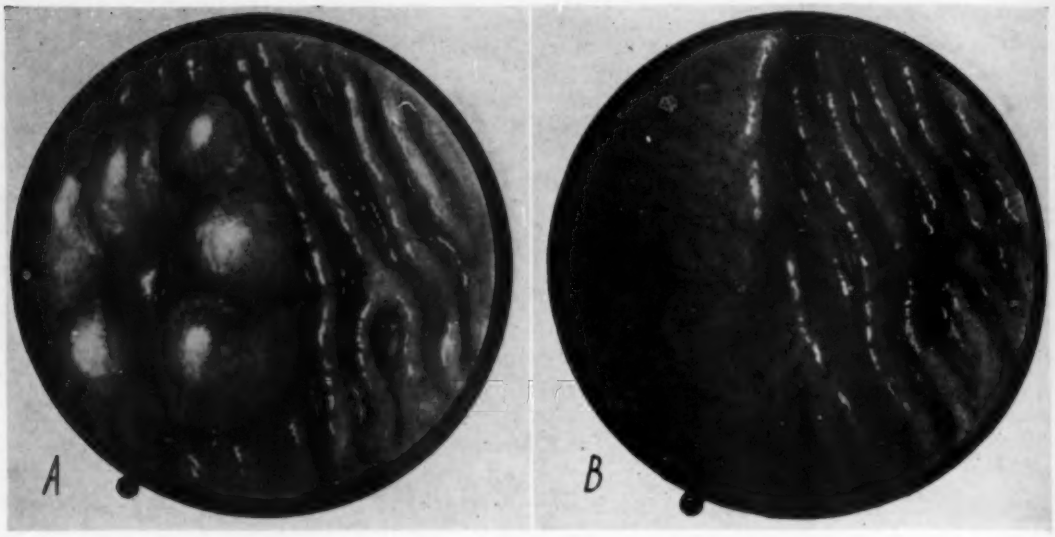

Fig. 3. Case 1. Secondary lymphosarcoma of stomach. Gastroscopic appearance. *A*, before treatment; *B*, after roentgen therapy.

nodules. The entire area was estimated as measuring 4 to 5 cm. in diameter (Fig. 3*A*). The patient then received 2,850 r (measured on the skin) in twenty-seven days with 200 kv. over a left upper abdominal field. Roentgenoscopy on September 16, 1941, five days after the end of this treatment, showed practically a normal stomach (Fig. 2*B*). Gastroscopy toward the end of treatment on September 9, 1941, showed practically normal mucosa (Fig. 3*B*). There was only a slight depression at the former area of ulceration which was covered with a smooth mucosa and was limited by a somewhat raised ridge. This would not be recognizable if one had not known that at this place a lesion had been previously present. This patient returned home in a hopeless condition due to progression of the general spread of the disease.

A strikingly similar case was reported by Kessler.[1]

K. H., male, aged fifty-six. In February, 1932, he noted discomfort in the throat; in May, 1932, he noted a swelling of the left side of the neck. In July, 1932, there was an ulcerated tumor replacing the left tonsil extending into the soft palate and tongue and extending along the lateral pharyngeal wall down to the level of the vallecula. There were walnut sized lymph nodes in the carotid triangle. Histopathologically this was a retothel sarcoma. He received fractionated irradiation between March 11 and 27, 1932, and the primary tumor and lymph nodes disappeared. In October, 1932, the patient complained of a burning sensation along the esophagus and pain behind the sternum. Roentgen examination on March 9, 1933 (Fig. 4) showed an irregular filling defect just below the cardia extending into the smaller curvature in its upper third. In the region of the fundus the tumor was recognizable as a soft part shadow extending into the greater curvature. There was a filling defect the size of a hen's egg in the anterior third of the greater

Fig. 4. Secondary lymphosarcoma of stomach; before treatment (from Kessler[1]).

curvature. Three weeks later the patient was admitted again because of increased difficulty in swallowing. He received irradiation over one anterior and one posterior field, 360 r to each field. There was marked improvement of the subjective complaint. Examination two weeks after this treatment showed only a slight irregularity in the region formerly found to be invaded, and examination after two months showed that the extensive mucosal infiltration in the proximal part of the stomach had completely disappeared. The stomach was then practically normal.

In September, 1933, the patient again had complaints in the abdominal region with normal roentgen findings. One could feel on the right side of the spine at the level of the umbilicus a resistance which was interpreted as a retroperitoneal infiltration. This was irradiated and the patient improved again. In February, 1934, he showed an acute abdominal picture and died within a few days. Autopsy was not done.

A most remarkable case was reported by Schindler[3] and Renshaw.[2]

The patient was a female, aged fifty-one. Tonsillectomy in May, 1932, for salivation. She was first seen in November, 1932, with the complaints of swelling in the neck, which had been present for two years with little change in size, loss of 20 pounds of weight in one and a half years in spite of fairly good appetite and shortness of breath. There was a firm swelling

Fig. 5. Secondary lymphosarcoma of stomach. Roentgen appearance before treatment (from Schindler[3]). (Reproduced with permission of the author.)

Fig. 6. Secondary lymphosarcoma of stomach. Gastroscopic appearance before treatment (from Schindler[3]). (Reproduced with permission of the author.)

about 4.5 cm. in diameter below the midportion of left mandible. A group of firm, discrete cervical nodes was easily excised with the submaxillary gland in toto. These showed microscopically a lymphoblastoma with disappearance of the lymph node structure.* No mediastinal lymph nodes were found on roentgen examination but the patient received a daily dose of 393 r through a 15 by 15 cm. portal over the chest on three successive days. Following this she felt well and gained weight.

In August, 1934, she again complained of shortness of breath. Roentgenogram of the chest showed a questionable evidence of lymphadenopathy and additional roentgen therapy was given through a 20 by 20 anterior chest portal with a daily dose of 306 r for three days, followed two months later by a daily dose of 314 r for three days through a posterior portal. Shortness of breath disappeared and she remained well for sixteen months.

In January, 1936, she reappeared with the complaints of an epigastric pain of one month's duration. At that time the roentgen examination of the stomach revealed enlarged gastric rugae not obliterated by pressure (Fig. 5). The conclusion was reached that there was a submucous infiltration which had not broken through the mucosa. On gastroscopic examination the angulus was found to be the site of marked changes. It was a scalloped nodular curve with a white ulceration toward the posterior wall. The musculus sphincter antri was cord-like and nodular. It contained a greenish-gray linear ulceration about 2

* Dr. Schindler kindly sent us a slide for review which we would diagnose as a small cell lymphosarcoma.

cm. long and 3 mm. wide. There was a small hemorrhagic spot on the greater curvature of the antrum in a swollen mucous membrane without folds or nodes. In the lesser curvature of the body just above the angulus there were many large nodules. The upper part of the posterior wall was normal (Fig. 6). The patient received five treatments, each of 200 r, through a 20 by 20 anterior abdominal portal, and three treatments likewise, each of 200 r, through a posterior portal. One month later the gastroscopic picture was found to have undergone a spectacular change. The stomach was almost normal, the angulus was smooth and the larger nodes and ulcers had disappeared. The roentgen appearance also was found to be almost normal. Three months later the patient felt better than she had for years. We were informed by Dr. Schindler that *this patient is still in good condition*, September, 1941; this means nine years after the lymph nodes in the neck were removed and *five and a half years after the stomach lesion was treated by roentgen irradiation.*

Our case and that of Kessler show a striking similarity and the sequence of events seems to leave little doubt as to the pathological interpretation of the stomach lesions as secondary foci following the local sterilization of a primary lymphosarcoma of the pharynx. The third case, that of Schindler and Renshaw, is most remarkable because of the long duration of the disease and the freedom of symptoms for more than five years following the treatment with small amounts of radiation to the roentgenologically and gastroscopically demonstrated stomach lesion. Whether in this case the primary focus was also located in one of the tonsils which were removed six months prior to the first observation is a matter of conjecture. We have seen cases of lymphosarcoma of the cervical nodes following a tonsillectomy in which a careful history of the clinical complaints previous to tonsillectomy justified the assumption of an unrecognized primary focus in the removed tonsil. Although the long freedom of symptoms in a primary lymphosarcoma of the tonsil with demonstrated spread beyond the regional lymphatic area is highly unusual it seems that there are cases in which apparently small (and even presumably insufficient roentgen-ray doses) have produced long intervals of good health (Taylor). We are still far from understanding the biology and the gamut of clinical pictures of the disease we call "lymphosarcoma."

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A PRENATAL DIAGNOSIS OF OSTEOPETROSIS*

By E. L. JENKINSON, M.D., W. H. PFISTERER, M.D.,
K. K. LATTEIER, M.D., *and* MARY MARTIN, M.D.
St. Luke's Hospital
CHICAGO, ILLINOIS

THE intrauterine diagnosis of osteopetrosis by means of roentgenograms is uncommon. One of 141 cases of osteopetrosis in the medical literature had a roentgenological diagnosis in utero.[7] Subsequent study of this patient at the age of six years revealed little evidence of osteopetrosis.[8]

Necropsies and roentgen examinations have demonstrated extensive osteopetrosis in the neonatal period.[3,4,5,10]

CASE REPORT

The case presented occurred in a colored female, aged twenty-nine, para I, gravida II, and pregnant six months. Fainting spells, nausea, vomiting, and albuminuria began in the first trimester. Repeated blood Wassermann examinations were negative. An unusual increase in weight and abdominal distention were found at the fifth month antepartum examination. There was progressive abdominal enlargement in the next month despite a salt free diet and restricted fluids. Loss of fetal heart tones and palpable fluid wave suggested polyhydramnios with a multiple pregnancy or monstrosity.

Roentgen Examination. On April 6, 1942, the mother was brought to the Roentgen Department for examination. She was very large and multiple pregnancy was seriously considered. Roentgenograms were made in the anteroposterior and right lateral positions. The films revealed a single small fetus and an exceedingly large uterus, undoubtedly due to polyhydramnios. The placenta was located on the posterior uterine wall. The mother's bones appeared normal and the pelvic inlet was within normal limits. Considering the size of the fetus, there was ample room for delivery.

The films revealed the fetal head to be located in the right upper quadrant, well anteriorly. The breach was located in the pelvis. Practically all the bones of the fetal skeleton were unusually dense and wide. The narrowing of the medullary canal of the long bones could be definitely seen in the prenatal films. The thick cortex encroached upon the medullary cavity. The bones of the extremities and the ribs were about twice the normal width and were marble like in appearance. The outlines of these bones were regular and quite sharply defined. No periosseous thickening or swelling could be seen. The metacarpals, metatarsals, and phalanges of the hands and feet could be easily demonstrated and were sclerotic. The carpal and tarsal bones could not be identified. The entire spinal column showed increased density with practically complete development of the bodies and processes. The ilia and ischia could be easily outlined in the lateral view and were of increased density. We were unable to outline any of the epiphyses of the long bones in the prenatal films. The skull presented many areas of increased density. The bones of the base of the skull which are laid down in cartilage and the bones of the face which are membranous in origin were similarly involved. The supraorbital ridges (frontal bones) were unusually dense. Examination of the bones with a magnifying glass revealed marked increase in density, but the bones were not entirely homogeneous. They seemed to be slightly on the granular side. An interesting finding was the calcification seen in the upper half of the fetal abdomen which we thought due to calcification in the kidneys. Later roentgenograms of the fetus after delivery and postmortem confirmed our belief. *Prenatal Diagnosis:* Osteopetrosis; congenital lues should be ruled out.

One week following the roentgen examination, the pregnancy was terminated and a macerated fetus was delivered. Photographs and roentgenograms of the fetus were made immediately following delivery. The fetus was 36 cm. long, 11.5 cm. anteroposterior diameter, and 12.5 cm. lateral diameter.

The roentgenograms made of the fetus following delivery showed marked swelling of the soft tissues of the skull and an unusually large abdomen.

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FIG. 1. Photomicrograph of decalcified humerus showing calcification of the osteoid tissue and reduced marrow spaces.

The parietal bones were slightly increased in density and were of rather peculiar construction. Perpendicular striae of bone extended outward from the primary center. The striae were well separated as they neared the peripheral sutures and were very sharp. The posterior parts of the frontals and the entire occipital bone showed this same pattern extending outward from the primary center. The bones of the base of the skull were very dense and quite homogeneous. The sella was poorly defined and flat. The facial bones were dense and broad and slightly mottled.

There was no evidence of the epiphyses of the upper or lower extremities. The carpal bones of the wrists were not present and only the center for the calcaneus was present in the feet. The general roentgen findings are similar throughout the entire skeleton: namely, increased density, widening of the cortex, narrowing of the marrow cavity, While the bones are definitely thickened, there is not a complete homogeneity. The trabeculae are not present, but there are small areas of mottling due to less dense bone. The cortical portion of the bones is not smooth. Irregular areas are present, especially in the extremities. The ribs are straight, predominantly dense, but do show some mottling. The metaphyses of the ends of the long bones are smooth and straight. No periosteal reaction is discernible. Calcification is present in the upper abdomen which we believe to be in the kidneys. The chief roentgenological characteristics are as follows:

1. Increased density of practically all of the bones. The increased density is generalized.
2. Widening of all the long bones, especially the tibiae and ulnae.
3. Fine mottling of the long bones.
4. Narrowed medullary cavity.
5. Thickening of the cortex.
6. No periosteal thickening.
7. The base of the skull is exceedingly dense. The sella is flat.
8. Increased striae in the parietal, frontal and occipital bones.
9. Calcification of the kidneys.
10. No periosseous thickening.

The bones of the mother and a half-sister of the fetus were normal in the roentgen examination.

Pathological Findings. The pathological findings in this case are discussed under three headings: (1) The fetus as presented after delivery; (2) the bleached bones of the skeleton after digestion of the soft tissues, and (3) the histological preparations of decalcified bone not previously included in the digestion. The description follows:

The tissues of the body of the female fetus, estimated at six months intrauterine age, were

FIG. 2. Photomicrograph of decalcified femur showing heavy trabeculae and fibrous tissue in the marrow spaces.

markedly macerated and hemorrhagic. Deposits of calcium seemed to outline the pyramids of the kidneys. Other viscera had autolytic changes. The long bones of the extremities, the ribs, the vertebrae, the bones of the cranium, and the bones of the face were greatly thickened and calcified.

The soft parts were digested with a 1 per cent NaOH solution, the bones recovered and bleached. They were chalky and fragile, but heavy and much larger than usual. The bones of the calvarium consisted of rather soft bone with no myeloid. In the large flat bones delicate spicules radiated from a thick spongy central portion. The occipital bone had a thick heavy central portion. The lateral portions were radiating spicules. The frontal bone was particularly heavy. The supraorbital ridge was thick and the supraorbital foramen had a diameter of 1 mm. The supraorbital plate had a thickness of 3 mm. The bone forming the floor of the anterior fossa was thick and porous. The pyramid of the temporal bone was heavy, dense, and the canals and foramina were prominent. The pyramid portion was 1.5 by 1.2 cm. The squama were thick and heavy. The zygomatic processes were 1 cm. in length and 0.4 by 0.4 cm. in their other dimensions. The short styloid processes were ossified. The thick greater wings and leaf-shaped lesser wings were well formed. The dorsum sellae were small but ossified. The nasal bones were well developed thin plates of chalky bone. The ossicles were about three-fourths of adult size and were well developed. The glenoid processes of the scapulae were completely ossified and were each about three-fourths the size of the remainder of the scapula. The hyoid bone was not identified. The coracoid processes were heavy but short. The mandibles were thick and heavy. The clavicles were 2.5 by 0.5 by 0.5 cm. There was a large heavy manubrial plate and two slightly smaller masses believed to be bones of the body of the sternum.

The large long bones were thick and heavy. The enlargement was diffuse. The fibula and ulna were much thicker in proportion to the radius and tibia than the normal relationship. The humerus was 2.5 cm. long. The central portion had a diameter of 1.2 cm. and the base

Fig. 4. Photograph of the macerated fetus.

Fig. 3. Lateral view showing fetus in utero; dense, widened, and thickened bones.

FIG. 5. Roentgenogram of the fetus, showing the increased density of the bones of the upper and lower extremities, ribs, spine, face.

roughly tapered to a diameter of 0.8 cm. at the lower end and 0.9 cm. at the upper end. At the diaphysis were transverse lines. The epiphyseal edge was rough and irregular and the bone here crushed easily. The radius was 2.5 cm., centrally it had a diameter of 0.8 cm. The shaft was diffusely enlarged. The diameter was approximately 0.7 cm. and the distal end was 0.5 cm. Five millimeters from the end of the bone was a transverse ridge and at the upper end were similar less distinct transverse lines parallel to the epiphyseal line. The ulna was slightly smaller and diffusely enlarged. It had a diameter near the center of 0.7 cm. The proximal end was 0.4 cm. in diameter and distally 0.4 cm. in diameter. No carpal bones were identified, but many irregular fragments remained and some of these probably represented carpal bones. The metacarpals were thick and much less chalky than the other bones. The largest was 1 cm. It was narrow near the center and flared at each end. Four phalanges were identified, grossly similar to the metacarpals. The cortex was much firmer than that of the other bones. The femur was 3.7 cm. long and diffusely enlarged. Near the center the shaft had a diameter of 1.3 cm. There were longitudinal lines at each end where the bones had a ruffled appearance and there were at each end faint transverse lines parallel to the epiphyseal line. The epiphyseal surface was rough and irregular. Proximally the diameter was 1 cm. and distally it was 1.2 by 0.8 cm. The tibia was grossly similar. It was 3.5 cm. long. The greatest diammeter at the upper third was 1.2 cm. At the proximal end the bone was 1 by 0.8 cm. and the epiphyseal surface was rough and irregular. Distally it was 0.7 cm. The fibula was 2.7 cm.

FIG. 6. Roentgenogram of the fetus, lateral view, showing calcification in the kidneys, increased density, and widening of the bones of the upper and lower extremities, vertebrae, ribs, and base of the skull, and a large pendulous abdomen.

long and diffusely thickened. The markings were similar to the other bones. At the proximal end the diameter was 0.4 cm. and distally it was 0.4 cm. Centrally it was 0.8 cm. in diameter. The ribs were heavy spongy bones with greatly reduced marrow cavities. The largest, along its convex edge, was 3.5 cm. The first ribs were well developed. The bodies of the vertebrae were heavy solid masses. The largest recovered were 0.8 by 0.5 by 0.5 cm. The lamina of all the vertebrae were thick. The spinous processes were well developed and the thoracic ribs had well developed thoracic processes. The wings of the pelvic bone were large and heavy. The margins were ruffled. The ischia were heavy. The ischial tuberosity was well developed. The foramen had a diameter of 1 mm.

Histopathological Findings. Bone "A": Longitudinal sections of the decalcified femur had at the diaphysis a zone of unmodified hyaline cartilage penetrated by a few blood vessels. There was a variable amount of lime in the cartilage matrix here. Beneath this was a narrow zone of calcified cartilage where the large swollen vesicular cells in rows were separated by narrow walls of more basophilic matrix. The region beneath had cartilage erosion and endochondral ossification. This was irregular in extent. Narrow spicules of calcified cartilage were surrounded by wide zones of osteoid tissue. Deeper, where the marrow cavity should be present, were wide trabeculae of osteoid tissue, some with masses of persisting calcified cartilage in their centers. Near the center of the shaft was marked irregular ossification of this osteoid tissue. The trabeculae here were wide, markedly irregular and compressed the marrow. There was little difference between the compacta and spongiosa except in the nature of the elements found in the reduced marrow spaces. Periosteal bone formation was active but there was here an abnormal amount of osteoid tissue with irregular lime deposition. In the narrow marrow spaces between the thick peripheral trabeculae was a cellular fibrous tissue. Here were many persisting masses of unchanged hyaline cartilage. There was no fat in the small marrow spaces. Centrally the relatively small amount of hematopoietic tissue was compressed by masses of cartilage matrix undergoing resolution and lysis. The usual discontinuous layers of osteoblasts were along the margins of the trabeculae but only a few osteoclasts were present. The small amount of hematopoietic tissue contained mainly young cells of the erythrocytic series, many adult macrocytes and large nucleated red cells. There were some young cells of the granulocytic series, very few of them acidophilic. No megakaryocytes were found.

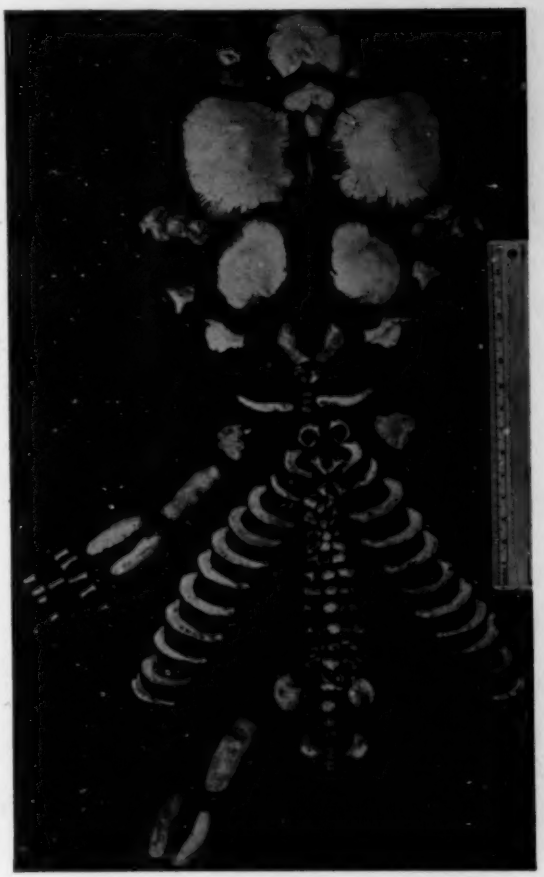

Fig. 7. Photograph of the disarticulated skeleton after removal of the soft tissues.

Section "B": The radius and ulna resembled those described in the femur. Here, however, the persistence of calcified cartilage in the trabeculae was more marked. The wide dense trabeculae had narrow margins of intensely staining osteoid tissue. The marrow spaces contained in a fibrous stroma a moderate amount of hematopoietic tissue.

Section "C": The humerus had essentially the same changes. The dense trabeculae of the spongiosa had more marked ossification and the osteoid tissue was less in amount. The marrow here was mainly loose vascular fibrous tissue. The kidney tissues were markedly autolyzed. However, outlining the calyces and in the walls

of the larger blood vessels near the pelvis were large irregular deposits of calcium.

Diagnosis. Macerated premature fetus; osteosclerosis fragilis generalisata (Albers-Schönberg's disease); calcification of renal tissues; postmortem autolysis of the tissues.

No spirochetes were found in sections of the liver stained by the Levaditi method.

To summarize the outstanding changes in the bone tissues of this case: Grossly, the long bones were diffusely thickened and heavy. Near the diaphyseo-epiphyseal lines were transverse ridges. Particularly well marked at the ends of the tibia were longitudinal striations giving a "ruffled" appearance to the bone. The ulna and fibula were much thicker in proportion to the radius and tibia than the normal relationship. The membrane bones of the face and cranium were less involved than the cartilaginous bones. The large flat bones were practically normal. The marked development of the supraorbital ridge, large size of the pyramids and ossification of the styloid processes were noteworthy. The bone tissue was chalky and fragile. Histopathologically the disturbance seemed to be in the ratio between bone formation and absorption. The periosteum was intact. There was endosteal increase in density and thickness. The epiphyseo-diaphyseal lines of the long bones were ragged but epiphyseal development was normal. The sclerosis seemed to have occurred after the centers developed. There was increase of cortical bone with widening and broadening of the trabeculae. The spongiosa was obliterated and the marrow spaces were reduced. Much of the marrow contained fibrous tissue. There was an abnormal amount of osteoid tissue in the centers of the shafts. The significance of calcium material outlining the renal pelvis was difficult to determine. The soft tissues were badly macerated and the finer structure altered by autolysis. No parathyroid tissues were identified.

DISCUSSION

Roentgenological features of osteopetrosis were first described in 1904 by Albers-Schönberg,[1] who called the condition "marble bones." The term "osteopetrosis" was suggested by Karshner[5] on the basis of bone petrifaction. Pirie[8] demonstrated that the density and drilling qualities of the involved bones resembled chalk rather than marble and called them "chalky bones." The etiology of osteopetrosis is not known. The rôle of chronic infection, avitaminosis, and anomalies of osteogenesis are not well defined. Péhu, Policard and Dufourt[6] suggested a parathyroid tumor in their case as the etiological factor. Pugsley and Selye[9] injected parathyroid hormone in rats and observed an initial increased calcium excretion subsequently followed by a normal or subnormal excretion. This acquired resistance to experimental hyperparathyroidism could be converted into a condition closely resembling marble bones if the administration of parathyroid were continued. The osteoclastic reaction (osteitis fibrosa) changed over to an osteoblastic one (marble bone formation) at the same time that the increased calcium excretion and hypercalcemia returned to normal limits.

Péhu, Policard and Dufourt,[6] Schulze,[11] and Alexander[2] found deposits of calcium in tendons, myocardium, blood vessels, skin, and in the kidneys, and believed that parathyroid hyperactivity was significant. Parental consanguinity and familial tendencies have frequently been reported. Sex and race are not important. Most reported cases have been diagnosed before puberty. Pirie[7] believes that the disease starts at the epiphyseal line where alternating transverse bands of greater and lesser densities are so common that they are considered pathognomonic. Similar findings, however, may be found in chronic illness due to nutritional growth arrests. The pathogenesis of the poorly differentiated, unorganized amorphous bone is not decided. The marrow cavity is replaced by spongiosa having a marked increase in number and thickness of individual trabeculae, between masses of persisting calcified cartilage. The lamellae of the cortex are increased in number and are more compact. The pathogenesis may result from abnormalities in the hyaline matrix, the osteolytic mechanism, or failure of metaplasia from fibrous to osteoid tissue. Various authors disagree as to the rôle of osteoblasts and osteoclasts. In the case presented the usual discontinuous layers of osteoblasts were along the margins of the

trabeculae but only few osteoclasts were present. Osteopetrosis may be suspected clinically by its secondary manifestation. The diagnosis is usually made by roentgen studies.

All the bones of the skeletal system are affected. The vertebrae, pelvic bones, base of the skull, and ends of the long bones are most extensively involved. The hard cortical bone is more than twice the usual thickness and there is condensation and broadening of the bony trabeculae. The spongiosa and marrow elements may be obliterated by the encroaching compacta and replaced by fibrous tissue. The hyperplastic bone growth is entirely endosteal. The periosteum is rarely involved.

The ossification centers appear at the normal time and epiphyseal unions are only slightly delayed.

The chemical analyses of the bones have failed to reveal any characteristic changes in their calcium, phosphorus, magnesium, or carbonate content. The calcium and phosphorus content of the blood serum is normal. The osteosclerotic or myelophthisic anemia accompanying the disease probably results from encroachment on the marrow elements by the compacta. Metaplasia of extramedullary hematopoietic centers may account for the enlargement of the liver, spleen, and the lymph glands.

DIFFERENTIAL DIAGNOSIS

A careful history is most important in the differential diagnosis of osteopetrosis. A complete roentgen examination of the skeleton is also imperative.

Congenital syphilis probably presents the most difficult diagnostic problem. In congenital syphilis there is a marked thickening of the periosteum and sclerosis of the bone, but there are also areas of destruction in the region of the metaphyses. Syphilis rarely attacks the bones of the base of the skull, while osteopetrosis usually involves this portion of the skeleton. Serological studies are very important in the differential diagnosis.

Osseous changes in leukemia are not uncommon and were originally described by Hueck in 1879. However, the changes are predominantly infiltrative and destructive rather than proliferative. When sclerosis does appear, it is not so generalized.

In certain parts of the world, chronic fluorine poisoning presents changes which may be confused with osteopetrosis. Here the history is of great importance. The offspring of persons in any way associated with fluorine may show changes of the sclerotic type. In fluorine poisoning the architecture of the bones remains unchanged and calcium fluoride crystals can be identified histologically in the haversian canals. The adjacent soft tissues show osteophyte formation with calcification of the intervertebral ligaments and periosseous deposits.

Some of the more uncommon conditions such as condensing osteitis of Sicard, eburnizing osteitis of Putti, ivory vertebra, or leontiasis ossea, while they may cause some confusion, are usually localized and do not present the generalized sclerosis seen in osteopetrosis.

Paget's disease may present a difficult problem in older patients. However, the changes in the skull, pelvis, and long bones of the extremities are usually quite characteristic. The bones are not homogeneous and the trabeculae instead of being absent are very prominent and thickened

Chronic metallic poisoning such as lead or phosphorus may cause diagnostic difficulties. The history, chemical analysis, and examination of the red blood cells are of great importance from a differential standpoint. When the irritating metals are withdrawn the patient's condition very often improves and the areas of sclerosis disappear. Osteopetrosis presents no peripheral neurological findings.

When multiple fractures occur in a patient, the differential diagnosis between osteopetrosis and osteogenesis imperfecta presents a problem. However, in the latter condition, the density of the bones is decreased rather than increased and trabeculae are present. Healing of the fractures

may take place in either condition. Moreover, marked deformities and bowing of the bones due to softening can be noted in osteogenesis imperfecta.

The course is frequently rapid and fatal. Involvement of the bones and foramina of the base of the skull may cause blindness, hydrocephalus, and hypophyseal dysfunctions. Mineral, vitamin, and endocrine therapy have been unsuccessful.

SUMMARY

1. A case is presented of prenatal osteopetrosis diagnosed roentgenologically and confirmed by necropsy.

2. A complete review of the literature reveals no confirmed prenatal diagnosis of osteopetrosis.

3. The skeletal changes reveal that cartilaginous and membranous bone show similar involvement.

4. From the review of the literature and the evidence presented in our case, osteopetrosis undoubtedly originates in utero and when accompanied by hydramnios, the fetal mortality is high.

5. It is not uncommon for patients with osteopetrosis to reach adult life.

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GHON'S TUBERCLE

RE-EVALUATION OF A CONCEPT*

By ROBERT G. BLOCH, M.D.

CHICAGO, ILLINOIS

OVER twenty-five years ago Ghon[5] published his studies on primary tuberculous infection. Since that time the small calcified focus in the lung has played a dominant rôle in the clinical aspect and the epidemiology of tuberculosis, and the term, "Ghon's tubercle," has been universally accepted as signifying the calcified single or multiple remnants of a tuberculous lesion resulting from a primary infection acquired in childhood. This interpretation is made regardless of the age of the patient in whom such a lesion is found; its origin is placed back in the early years of life from the adolescent and senile age period alike.

It is the purpose of this paper to re-examine the soundness of that apparently so firmly established concept on the basis of more recent experience. As in other fields of medicine, the increasing importance of pathologic study through serial and large scale roentgenologic observations in the field of tuberculosis compels us to reconsider some aspects of our knowledge regardless of how securely they may seem to have been founded in the past.

Ghon examined tuberculous lesions in 184 children by autopsy in St. Anne's Hospital in Vienna. Of that number he described in detail his findings in 125 as to pathologic detail, number, size, and distribution of the lesions. Table I shows the age distribution of his patients. The oldest was fourteen years, the average age four years, with more than one-third of the individuals less than two years of age. Ghon made no attempt to apply his findings to tuberculous remnants found in the lungs of adults; apparently it was the widespread recognition which his work received, rather than his own interpretation of his findings which led to a practice of ascribing all calcified foci in the adult to childhood infection. Without adequate observations which could form an acceptable scientific bridge from childhood to the adult age, the calcified focus discovered at any age and Ghon's tubercle are now synonymous; the term in that meaning has become common in everyday medical practice.

TABLE I

AGE DISTRIBUTION OF LESIONS DESCRIBED BY GHON[5]
(184 autopsies; description of 125 examples)

Age Distribution:	Number	Per Cent
Younger than 2 years	47	37.3
2 to 5 years	43	35.0
6 to 10 years	27	21.4
11 to 14 years	8	6.3
	125	100.0

Youngest child aged 2 months.
Oldest child aged 14 years.
Average age—4 years.

A few authors[3,4,6] from different continents and studying tuberculosis in various races have pointed out that calcifications are found more frequently in old than in young individuals; in fact, that there is a steady rise in the frequency of such findings with increasing age. Ten years ago, in beginning our case-finding programs for tuberculosis,[1] we examined a group of 2,300 white persons composed of college freshmen, graduate students, faculty members and hospital personnel of the University of Chicago. The examinations were made partly by roentgenoscopy and partly by stereoscopic chest roentgenograms. There was the striking discovery that calcified tuberculous remnants were more frequent in the older group of indi-

* From the Frank Billings Medical Clinic, Department of Medicine, University of Chicago.

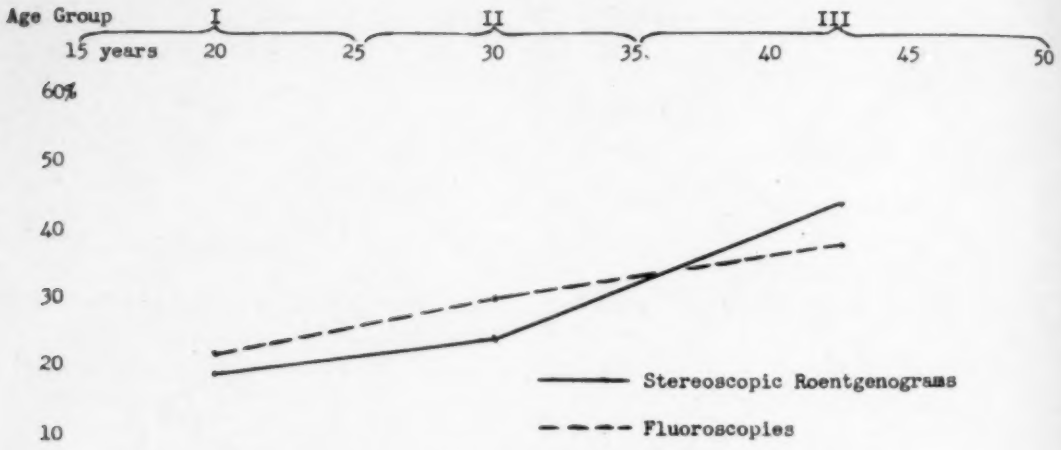

Fig. 1. Percentage of calcifications (Ghon's tubercles) in 2,300 white individuals of various age groups.

viduals. Figure 1 shows the steady rise through the various age groups by roentgenoscopic as well as by stereoscopic examination.

During the past three years we have conducted another case-finding program among the patients of the Clinic of Provident Hospital in Chicago introducing chest roentgenoscopy as a routine procedure in that institution.[2] The findings of

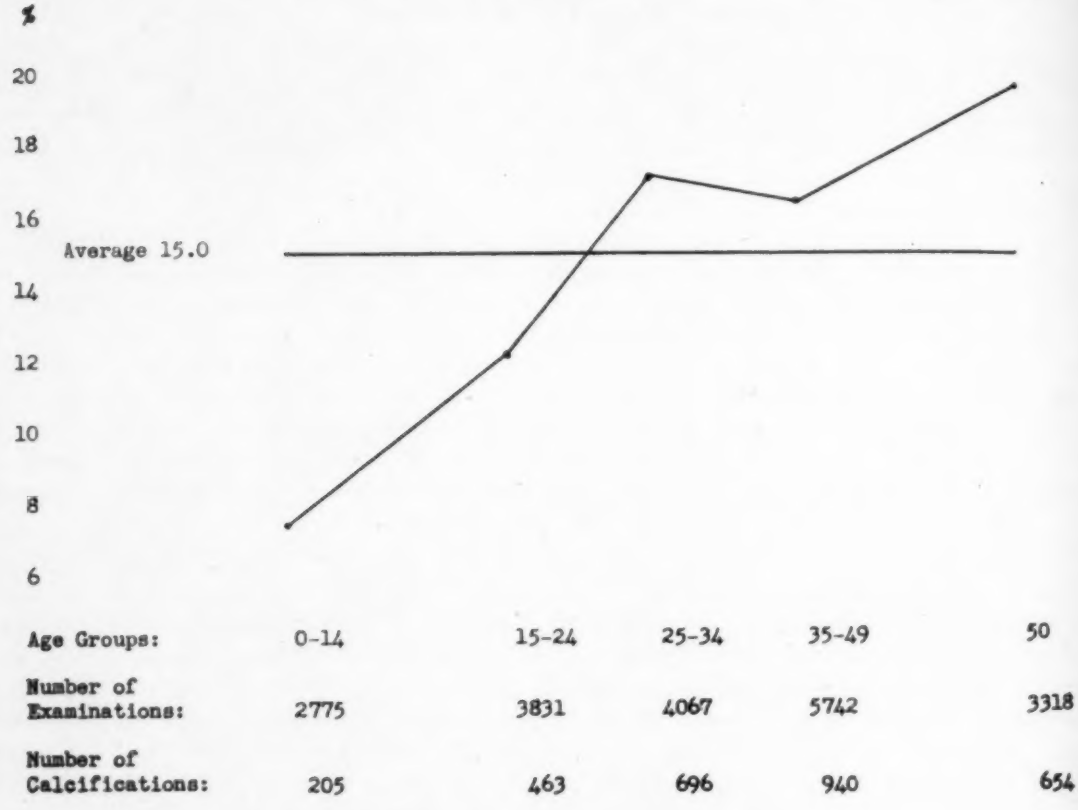

Fig. 2. Percentage of calcifications (Ghon's tubercles) in 20,000 Negroes.

calcified foci were recorded as to size, location, multiplicity of the lesion, and age of patient. In the first 20,000 Negroes of all ages who were examined there was again a sharp rise of the number of calcified foci with increasing age, as shown in Figure 2.

Realizing that a large number of such lesions, possibly their majority, are not discoverable by roentgenologic examination—the recorded average was 15 per cent—the groups are nevertheless representative. If failures of visualization could be corrected, the curve would probably rise still farther rather than decline, since failure of discovery is more likely to occur in the older and more obese groups than in the younger ones. It cannot be assumed that the majority of these foci would take from childhood to adulthood or even to middle age to reach the maturity of complete calcification. It was our observation, as it has been also that of others, that the average caseous lesion needs from six to eight years to reach a stage of calcification which makes it recognizable as such on roentgen examination. In childhood the period seems to be much less.

If the process of calcification consumes certainly less than a decade and if it is assumed to originate in childhood, why should we find so many more calcified tubercles among middle aged and old persons than in young adults and adolescents? In recent years much has been said about primary tuberculous infection in adults. With decreasing exposure of children to the tubercle bacillus, especially in some rural areas of the country. the occurrence of late primary infection has undoubtedly increased, but this shift is as yet of little significance in the general picture of tuberculous epidemiology, especially in the cities. Certainly in the middle aged and near-senile population the significance of first infection is to be denied. Primary adult infection, therefore,

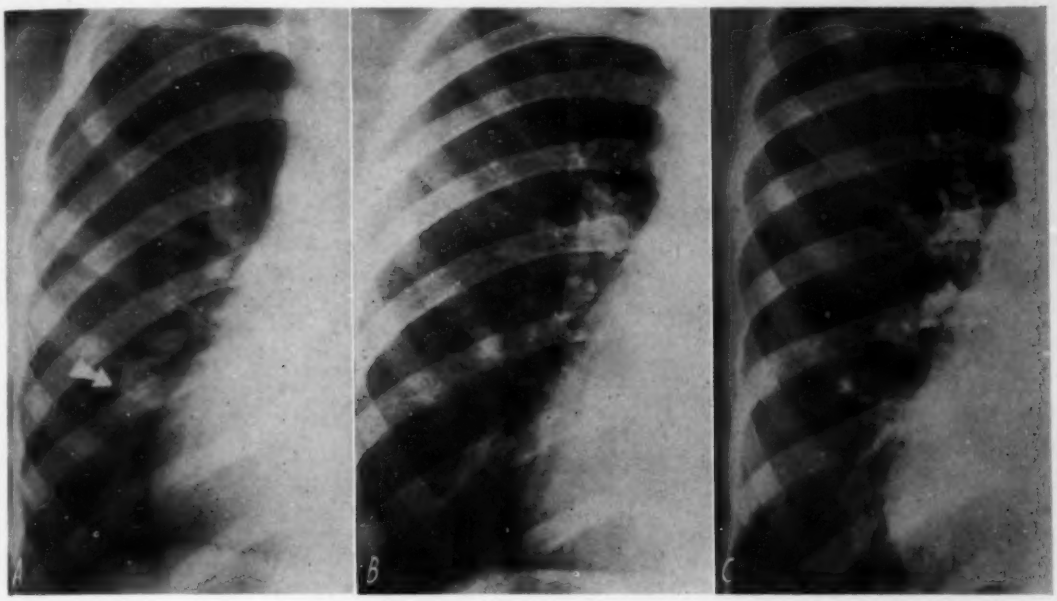

Fig. 3. Development of typical childhood (primary) focus. Unit No. 40866, B. T., female, aged six. Patient was exposed to infection from her mother who had pulmonary tuberculosis. *A*, taken in 1931, shows a fairly sharply outlined caseous focus near the left heart border. *B*, in 1933 the lesion appeared smaller, more sharply outlined, with a dense central focus representing calcification. *C*, in 1939 the peripheral area has been reabsorbed with the calcified nucleus remaining. Presumably the final stage was reached long before 1939 but no intermediate observations are available.

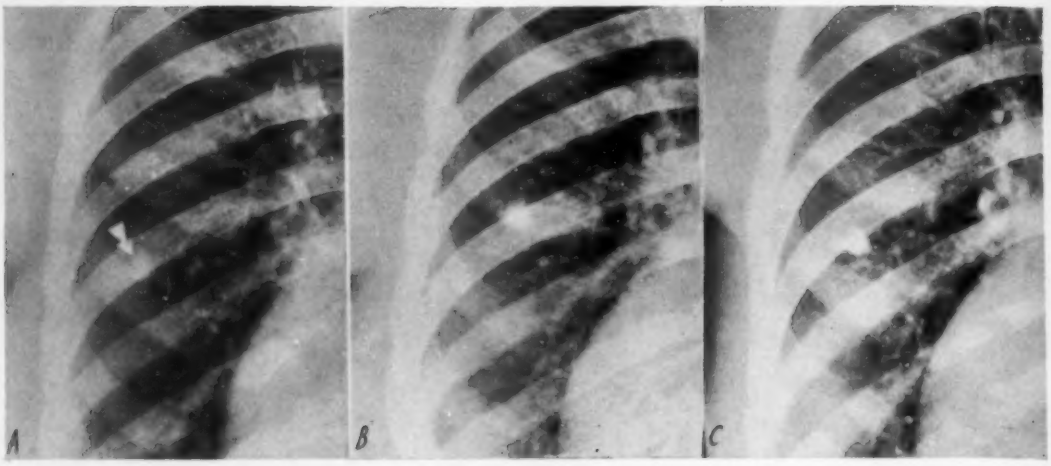

Fig. 4. Development of adult exogenous superinfection focus. Unit No. 8426, V. C., female, aged twenty-five. Patient was exposed to infection from her mother, who was found to have open pulmonary tuberculosis for some time before discovery of the daughter's focus. Patient was examined because of contact. A mild productive cough at the time of examination and recurring frequently after healing of the lesion was obviously related to upper respiratory infection. *A*, in 1929 an ill defined, small lesion was found in the left mid-lung field with round calcifying central area. *B*, in 1933 enlargement of the dense central area is still surrounded by a halo of lesser density. *C*, in 1936 there is complete calcification.

offers no answer to our question. The alternative is the assumption that a large number of calcified foci in the adult are not the remnants of a primary infection but rather the remnants of reinfection tuberculosis acquired during the adult age.

In recent years Ghon's student, Terplan,[8] in his studies on tuberculous foci has pointed out that reinfection can produce typical tuberculous complexes in the lung "heretofore considered as the characteristic sign of primary tuberculosis exclusively." In his anatomical observations he was not able to differentiate between the remnants of a second infection and the typical primary tuberculous focus. He stated that "the second complex . . . seemed to undergo the same regressive changes with encapsulation and chalky degeneration pointing to complete calcification as the ultimate result." Sweany[7] attempted the anatomical differentiation between the older and newer tuberculous foci on autopsy material and also demonstrated their development roentgenologically; the latter contribution showed that certainly in the roentgenogram the finished product of either variety is indistinguishable from the other.

Our own clinical and roentgenologic observations revealed great similarity and, in many cases, complete parallelism between the primary and assumed superinfection focus except for the previously mentioned difference in time which the average case of either variety consumes for the process of complete calcification (Fig. 3, 4, and 5).

In numerous examinations of persons who were known to have been exposed to recent tuberculous infection, mostly by family contact, small, usually caseous lesions were found in the lung fields on roentgen examination. Hardly any of these foci had caused symptoms, and they would not have been discovered at that stage but for a rule of the Chest Clinic to invite all contacts of our patients with active pulmonary tuberculosis to have a roentgen examination of the chest. Some of these small infiltrates were observed to disappear by reabsorption in the course of a few months or years. Others persisted

with slowly progressive encapsulation, deposition of calcium salts, and eventually calcification. It seems that many such patients, through excellent immunity, are able speedily to isolate the focus which has caseated after a localized infection has occurred in the lung tissue as the result of massive inoculation. The age of persons in whom these observations were made ranged up to sixty-seven years. In a few adults the formation of calcified foci was observed without any known preceding exposure to the organisms which could have caused the lesions by direct exogenous superinfection. In these patients the endogenous reinfection etiology can be assumed to be likely.

As in Terplan's observations, some of the lesions in question had developed in addition to pre-existing calcified foci in the lung parenchyma or the tracheobronchial lymph glands or both, thereby demonstrating their superinfection nature. From this it would follow that parenchymal calcifications found together with calcified glands may have resulted from an attack of infection different in time from that causing the development of the adenopathy. This would mean that the etiologic unity as to time, of a complex consisting of parenchymal and glandular involvement in the calcified state, cannot be taken for granted.

If the possible superinfection origin of the so-called Ghon's tubercle can be considered as established, it is only a step to the speculation that even a child's calcified focus may not be the remnant of a

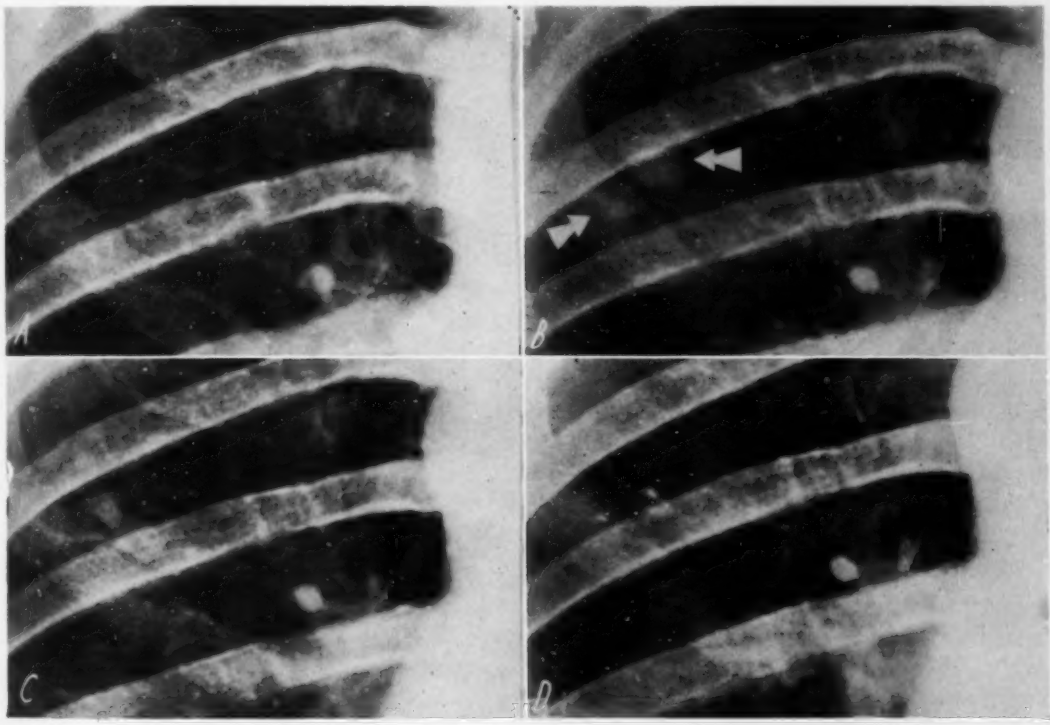

Fig. 5. Development of adult—possibly endogenous—reinfection foci. Unit No. 15600, M. P. H., female, aged thirty. Several members of the immediate family had pulmonary tuberculosis but there was no known contact for some time preceding discovery of the lesions. *A*, roentgenogram taken in 1929 on occasion of a general examination failed to show pulmonary involvement. *B*, in 1939 two irregularly shaped but sharply outlined foci of little density in the left subapical area. At that time patient had mild systemic symptoms. *C*, in 1933 the foci were more sharply circumscribed and of greater density. Patient was clinically well at that time. *D*, in 1937 there was complete calcification of the foci, then much reduced in size.

first infection in the strict sense of the word. Some of us have long abandoned the concept of a single inoculation from which primary lesions result, and prefer to speak rather of a primary infection period during which several or many inoculations with the tubercle bacillus occur, one of which, but not necessarily the first one, results in the petrified tubercle; in other words, even the true Ghon's tubercle of early life may be the expression of a reinfection superimposed on the truly first lesion which we know frequently is absorbed, leaving no macroscopic residuals.

CONCLUSIONS

It seems logical on the basis of such evidence that a re-evaluation of the so-called Ghon's tubercle or primary tuberculous calcification is needed. In the light of our present knowledge, the only justifiable interpretation that can be placed on the finding of a calcified tuberculous lesion by roentgen examination is that it represents the innocuous residual of a tuberculous infection, either a primary infection or reinfection at some prior time, either in childhood or adulthood, without its being possible to determine the time at which the infection occurred.

Therefore the term, "Ghon's tubercle" should either be dissociated entirely from the time element and applied to all small calcifying or calcified tuberculous foci regardless of age, or if it is to be retained as signifying the residuals of a childhood infection it should be applied only when the calcified residuals are found in the child.

SUMMARY

1. The childhood origin of all so-called Ghon's tubercles is to be doubted.

2. Through large scale pathologic and roentgen examinations, the greater incidence of calcified foci in higher age groups has been established.

3. The majority of such lesions originating during adult life can be traced to exogenous superinfection of individuals who are known to have been exposed to infection as adults.

4. Serial roentgenographic evidence of the development of calcifying foci in adults is presented.

5. They cannot be differentiated from childhood (primary) lesions.

6. The concept of the true primary nature even of the childhood calcification can be doubted.

7. The term, "Ghon's tubercle," should be dissociated from the time at which the infection occurred or should be limited to foci found in children only.

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TEN THOUSAND CHEST EXAMINATIONS WITH THE STEREOSCOPIC PHOTOROENTGEN UNIT*

By JOSEPH LEVITIN, LIEUTENANT COLONEL, M.C.
Roentgenologist, San Francisco Recruiting and Induction District
SAN FRANCISCO, CALIFORNIA

THE problem of tuberculosis in the Army is the discovery of the minimal lesions that exist without symptoms. Many of these lesions are latent and might remain so under ordinary conditions of life. In Army life, fatigue and a lowered resistance may activate these latent foci, so that the individual in question may become a casualty and a burden on the government for the rest of his life. It is estimated that each case of tuberculosis in the last war cost the government between $10,000 and $15,000, the total cost reaching over one billion dollars.

The best way to detect these latent lesions is by roentgen examination.[5,12] Physical examination alone is inadequate, for physical signs in most instances are lacking. Moreover, chest surveys by the roentgen ray are not new. The reader is referred to the excellent articles by Robins and Ehrlich[11] who examined 20,000 in New York City using an emulsion on a paper base; by Richards,[10] who reported on over 300,000 cases, examined for the Canadian Army using 14×17 inch films; and by Edwards and Ehrlich,[4] who reported on over 50,000 inductees and National Guardsmen in New York City using the paper roll. Pindell[6] recently reported a series of 2,107 cases using the photoroentgen unit and taking 4×5 inch single films. All agree that group survey by roentgen examination of the chest is satisfactory, the results justifying the work and expense involved.

The photoroentgenoscope used at this station is made by the General Electric Corporation. Films are taken stereoscopically. The apparatus and the technique of its use are described in the excellent articles by Potter[7,8] who collaborated with the General Electric Corporation in its development; by Lieutenant Colonel de Lorimier†,[2] who was instrumental in its development for the Army, and by Pindell.

In the past questions were raised respecting the diagnostic accuracy with which the 4×5 inch film could be used—such questions being directed essentially at the technical qualities of density, contrast, and detail, and the influence they have on the readability of a film. To obtain the best results with 4×5 inch film, time, experience, and improvements show that consideration must be given to the use of the proper type of developer and film and to the use of a fine, stationary grid.

In the first place ordinary developer would necessitate a long developing time which increases the chemical fog. High speed developer shortens the developing time so that six minutes at 65° F. can be used and chemical fog can be avoided.

Second is the use of the single coated film. It gives better detail because there is one image instead of the two present on the double coated film. The significance of this was pointed out by de Lorimier[3] who brought out the fact that we are dealing with light waves from the fluorescent screen to sensitize the emulsion on the film rather than roentgen rays. When the double coated film is used the light waves are refracted when passing through the front layer of film emulsion and through the film base. About 30 per cent of this light goes through the film, finally to become effective upon the back layer of emulsion. The blurred image of the second

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† Director of the Department of Roentgenology in the Army Medical School.

emulsion is superimposed upon the sharper image of the first emulsion which accounts for the considerable unsharpness of detail when using the old type roentgen films for photographing the fluoroscopic image.

Another advantage of the single coated film is the greater latitude and range in gradation of densities. This is true because there are two emulsions coated one on top of the other. Hence we are less apt to lose detail in the outer zone when the central zone is overexposed.

The arrangement of the lens in the camera is such that there is greater concentration of light in the central zone. This is seen on the old type film as a dark central area. The increased latitude in single coated films offsets this disadvantage to a great extent and the film shows a more even exposure. This film has less contrast than the old type double coated and requires the use of a stationary grid to diminish secondary rays and build up contrast.

All these factors tending to improve the film must be compensated for by increase in kilovoltage or milliampere-seconds. The miniature film takes about 10 kv. more than the conventional 14×17 inch film; the use of the grid requires either doubling the milliampere-seconds or another increase of from 10 to 12 kv. The single coated emulsion film also requires an increase of about 4 kv. All this throws a greater burden on the tube and shorter life must be anticipated than on the conventional roentgen-ray installation.

The diagnostic value of these smaller films has been excellent, and it is only in the exceptional case when the individual measures over 30 cm. that a 14×17 inch film is taken. It has never been necessary to take a 14×17 inch film in order to check a doubtful shadow. The stereoscopic shift giving two views clarifies doubtful shadows, throwing small shadows obscured by the ribs in one view into the interspace in the other. De Lorimier rated the 4×5 inch stereoroentgenogram of greater diagnostic value than the single 14×17 inch film. In his experience he found that early lesions of reinfection tuberculosis are made more conspicuous on the miniature films than when projected into the larger dimensions of the 14×17 inch film.

This increase in sharpness is easily understood when we realize that the grain of the fluorescent screen is reduced in proportion of 14×17 to 4×5 inch. This view of the greater efficiency of the 4×5 inch film is also shared by Christie[1] who states that for minimal lesions he feels more certain of their detection by means of two 4×5 inch films made with a tube shift than with a single 14×17 inch film of the best quality. Shifting of the tube serves to uncover portions of the lungs which may have been obscured by bones or other structures in the roentgenogram. It is the minimal lesion which is most significant. Large lesions can be easily demonstrated on any type of procedure. If the case should require further study, the stereoscopic film is available.

Another factor favoring the 4×5 inch film is that they can be interpreted with less fatigue for the roentgenologist. As de Lorimier states, the scope of the visual concentration is limited and a study of a 14×17 inch film is comparable to viewing 6 to 8 miniature films. This is an important factor in survey work where from 200 to 400 films are to be diagnosed daily. Viewing small dimensions requires fewer fields of visual concentration and the increased sharpness of densities in the lung makes them more conspicuous. His conclusion is that the miniature stereo films are best for a case finding procedure.

For diagnostic purposes, oblique and lateral views on conventional sized films can be obtained.

Diagnostic accuracy has been checked by others in comparative studies of the 4×5 inch film versus the 14×17 inch. Potter, Douglas and Birkelo[9] found the percentage of error as 2.6 on the 4×5 inch film among 271 cases checked by the large film. In nearly every instance the minimal lesions were superimposed over rib shad-

ows in the small film. This, of course, is obviated by the two views obtained with the stereoscopic shift. The reverse now holds true, a small lesion missed behind a rib in a single 14×17 inch film is thrown into the interspace by the different position on the stereoscopic film. Ezra Bridge (quoted by Pindell)[6] also reported on the examination of 1,000 patients at Iola Sanatorium with the 14×17 inch film and the small 4×5 inch film. Of the 130 minimal cases found, 2, or 1.5 per cent, were missed on the miniatures. At that time a system for producing or using the stereofilm was not available.

A strict comparison of results of interpretation of the 4×5 inch films with 14×17 inch films is difficult. If the results of one individual reading 4×5 inch films is compared with that of one reading the same cases of 14×17 inch films we must take into account the error inherent in the individual. No two individuals would read 1,000 roentgenograms alike, and even the same individuals would read the same 1,000 roentgenograms with some changes at different times. The factor of fatigue of the roentgenologist also enters. Richards, reporting on chest roentgen examinations of the Canadian Army found that 11 cases out of 328,325 were missed, or a percentage error of 0.003. In each instance the lesion was overlooked by competent men and all agreed the lesion was present when the roentgenogram was reviewed. This percentage is admittedly low but it is based on only review of those cases which subsequently showed active tuberculosis. They do not know how many were missed in the group that did not become active.

The accuracy of either type of case finding procedure cannot be judged by the results obtained if the same individual read a series of 4×5 inch films and a comparable series of 14×17 inch films on the same cases.

Unless the series is large, the roentgenologist could not help but carry a visual memory of the few positive and doubtful of the first series in his mind, and subconsciously look for them in the second series. No one, to date, has reported a series large enough to avoid such an error.

An idea as to the accuracy of the stereo 4×5 inch film as compared to the 14×17 inch film may be gained by a comparison of the percentages of reinfection tuberculosis found if the material is based on the same cross section of population. This has added accuracy if they are reviewed by the same individual.

Before the photoroentgen unit was established at this station, the men were sent to private roentgenologists for 14×17 inch single chest roentgenograms. I had the opportunity of reviewing 2,410 of these roentgenograms. The incidence of reinfection tuberculosis in this group was 1.2 per cent. This compares to 1.36 per cent found on the stereo 4×5 inch roentgenograms based on 10,000 cases examined at this station. This difference does not imply that the 4×5 inch films are 0.16 per cent more accurate. The sampling error in each group must be considered and their result compared.

The statistics of each group were analyzed by Dr. E. L. Lucia and her conclusion was that there is no difference in the effectiveness of diagnosis between the two types of film.*

* In sample I a positive rate of 13.6 per 1,000 was observed among 10,000 examinations made.

In sample II, the number of positives was 12.0 per 1,000 among 2,410 examinations.

The difference between these two rates is 1.6 per 1,000.

To determine whether or not this difference is significant, it is necessary to calculate the sampling errors for each of these rates.

The formula reads:

$$\sigma_{p_1} = \sqrt{\frac{p_1 q_1}{n_1}}$$

where p_1 (the chance of success) is 13.6 per 1,000 and q_1 (the chance of failure) is 987.4 per 1,000, or the difference between 1,000 and the chance of success: $1{,}000 - p_1 = q_1$.

By substituting the values for sample I, we have

$$\sigma_{p_1} = \sqrt{\frac{13.6 \times 987.4}{10{,}000}} = \sqrt{1.34} = 1.158.$$

The rate may be written as 13.6 per 1,000 ± 1.158.

Similarly substituting the values for sample II, we have

$$\sigma_{p_2} = \sqrt{\frac{12 \times 988}{2410}} = \sqrt{4.92} = 2.218.$$

The rate may now be written as 12 per 1,000 ± 2.218.

The formula for the sampling error of the difference of proportions is as follows:

$$\sigma_{p_1 - p_2} = \sqrt{\frac{p_1 q_1}{n_1} + \frac{p_2 q_2}{n_2}}.$$

By substituting the squares of the values obtained for the sam-

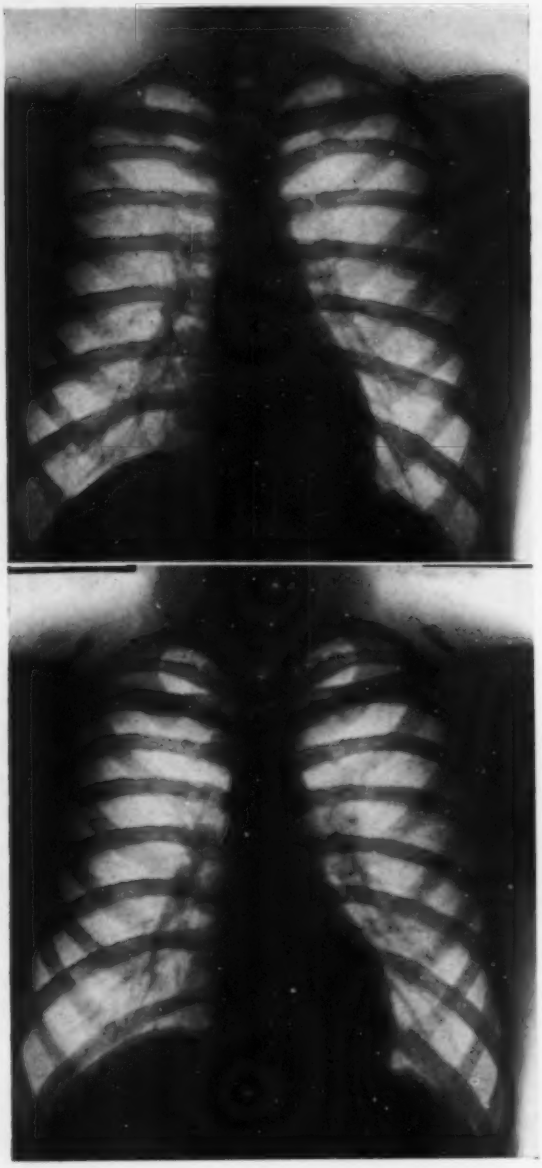

Fig. 1. Normal chest. Stereoscopic roentgenograms taken on a single 4×10 inch film; single coated emulsion. To be viewed on the orthostereoscope specially designed for the purpose. The image is magnified about twice by the stereoscope.

In addition to the accuracy of the diagnosis and less fatigue in its interpretation, another factor of importance to be considered where we are dealing with surveys of large numbers is the ease of handling the smaller film which requires less developing, drying space and storage room.

This report is based on 10,000 consecutive roentgenograms of chests of men coming for final type physical examination prior to induction in the United States Army. All have had a preliminary screen examination by their local draft board. Those obviously suffering from or being treated for conditions exempting them from the Army are not sent in. In addition to this group making up the series are a small number of those seeking enlistment. It can be stated that the group is made up of men considered as fit applicants for military duty. *Not one is receiving a chest roentgenogram because he requires it.*

The roentgenograms are interpreted as

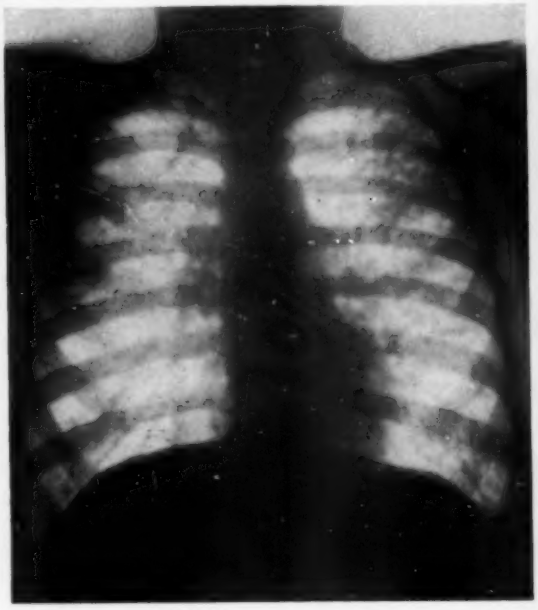

Fig. 2. The only complaint of this individual was laryngitis. The roentgenogram shows a large cavity measuring about 8 cm. in diameter at the right apex with nodulations and fibrosis of the right upper lobe. Fibrosis and nodulation involving the left upper lobe. The roentgenogram was taken on the double coated emulsion. In comparing with Figure 1, note the hazy outline of the vascular markings and the lack of sharpness of the ribs. The roentgenogram also shows more contrast, but poorer detail.

pling of p_1 and p_2, we find $\sqrt{1.34+4.92}=\sqrt{6.26}=2.5$

The difference between 13.6 and 12.0 which is 1.6 has been found to have a sampling error of 2.5, a value greater than the difference itself. From the standpoint of the statistical analysis it is customary to state the sampling error of the difference of 2.5 that the difference should be at least 7.5 to be signifiacnt, all other things being equal. A difference of 1.6 may therefore be said to have no significance whatsoever. Dr. E. L. Lucia.

Associate Professor of Biometry, Department of Hygiene, University of California.

to primary tuberculosis and reinfection type. All reinfection types are disqualified for unlimited service even though healed. The primary types with calcifications were accepted for the first 6,927 cases. A later ruling disqualified those with calcifications where there were more than five calcified hilar glands or where one has a diameter of 1.5 cm. or larger (measured on the 14 × 17 inch film). Also eliminated were those with parenchymal calcifications of more than five in number and where one measured 1 cm. in diameter or larger (14×17 inch film).* The cases with these calcifications, although rejected, are tabulated under calcified lesions.

All cases showing reinfection tuberculosis were grouped as to whether they appeared healed or active on the roentgenogram. It is admittedly dangerous ground to determine activity on the roentgen appearance of the lesion. The leaning was toward conservatism in the diagnosis of healed lesions. All lesions that were calcified, or showed sharply demarcated strand-like infiltration, were considered as healed.

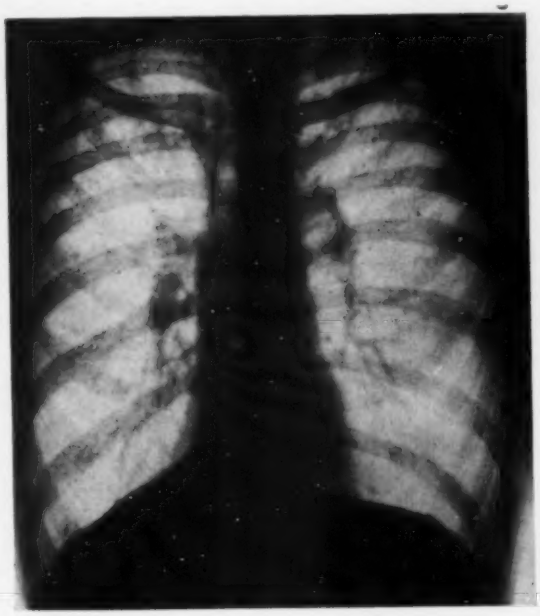

Fig. 3. This individual has been under treatment by various doctors for asthma for the past four years. No one had ever ordered a roentgen examination of the chest. The roentgenogram shows extensive fibrosis involving both lobes. The heart is small, with the mediastinal structures displaced to the right. (Single coated film.)

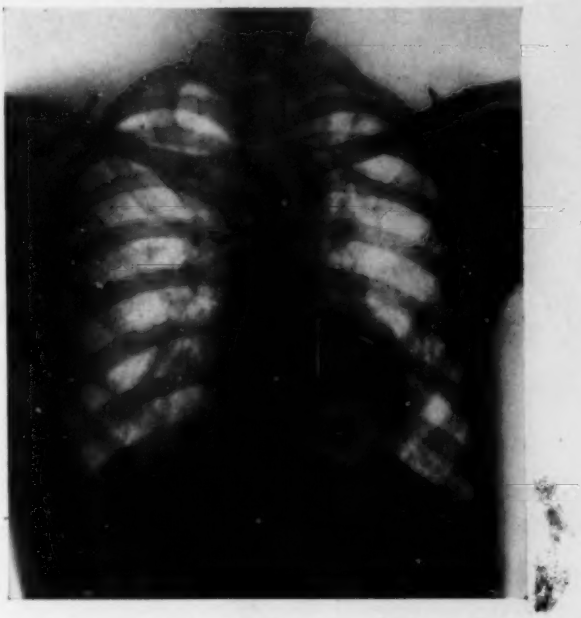

Fig. 4. This individual had no complaints or previous history of illness. He is a food handler of uncooked vegetables. Both upper lobes show considerable fibrosis. Cavity about 7 cm. in diameter at the left apex; one 3.5 cm. in diameter at the right apex. (Single coated film.)

All others were considered active, even though many are cases of arrested tuberculosis. This is the important group with which we are concerned from a public health standpoint and control of tuberculosis. The active and the arrested cases are the ones either spreading the disease or the ones likely to break down. The healed and calcified cases are of interest for statistical purposes. Active and arrested cases were the ones with soft nodulations, calcifications with periphery of lesser densities fading into the normal parenchyma and cavities.

The histories of all reinfection type tuberculosis were obtained and data noted as to whether or not the individual ever had any symptoms or signs pointing toward a chest lesion. Positive histories were pleural effusion, hemorrhage, cough, loss of weight, fatigue, and past treatment for tuberculosis. A history was called nega-

* Latest ruling allows ten calcifications in the parenchyma.

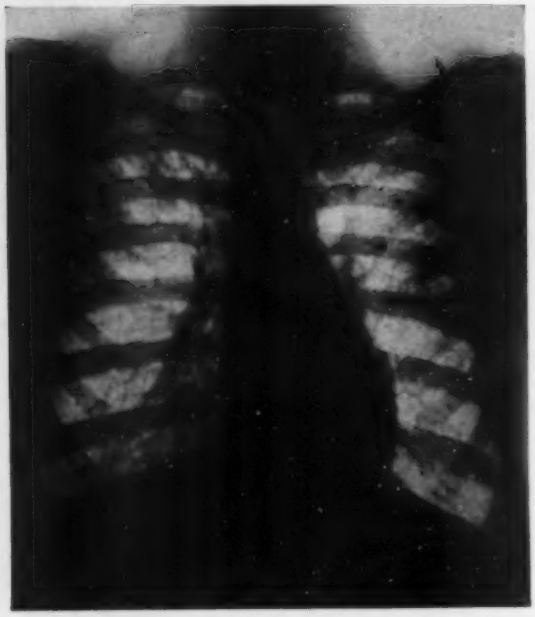

Fig. 5. This individual had no complaints or previous history of illness. He is a food handler of uncooked vegetables. Extensive nodulations and fibrosis of both upper lobes. Cavity about 2 cm. in diameter in the sixth interspace at the left axilla and one beneath the right clavicle. (Single coated film.)

tive when the individual had had no symptoms at any time referable to his chest.

It was astonishing to find the number of men with active tuberculosis having no suspicion of the disease. Fourteen had cavities and had been passed up as 1A in their routine physical examination. One had an extensive tuberculosis and his only complaint was a laryngitis (Fig. 2). Another had been treated for asthma for four years and had a fibrous tuberculosis. He had never been roentgenographed (Fig. 3). Also of interest were the number with cavities who were food handlers (Fig. 4 and 5).

Those rejected for chest conditions have their roentgenograms returned to their local draft board.* They are available to the men so that they may get proper treatment.

All rejected cases at this station are reported to the San Francisco Department of Health. In return they report out of town cases to the State Department of Health. Of the first 69 cases of reinfection tuberculosis, residents of San Francisco County, reported to the Department of Health, 8 were hospitalized, 10 were sent to their private physicians, and 8 were unable to be located. The rest were being treated in the clinic.

The results of the first 10,000 cases studied are shown in Tables I, II, III and IV.

* A new ruling sends roentgenograms of all rejected cases to the Director of State Selective Service.

Discussion

Those active cases of tuberculosis which have had a positive previous history should give us no concern. They are a problem of a closer follow-up system for those who have been treated, or further education of the public for those with symptoms to consult a doctor. A survey of medical facilities, to see if they are available for those with symptoms, should bring these cases under control. This number is the smallest of the whole group, only reaching 2 per 1,000.

Table I

	Total No.	No. per 1,000 Population
Reinfection tuberculosis	136	13.6
Calcifications, hilar and/or parenchymal	536	53.6
Other lung lesions	13	1.3
*Cardiac abnormalities	45	4.5
Dextrocardia	3	.3
Anomalies		
Vena azygos lobes	15	1.5
Cervical ribs	64	6.4
Anomalies of ribs; fused, bifid	19	1.9

* It is beyond the scope of this paper to analyze the cases of cardiac abnormalities; a subsequent report will tabulate the number of cardiac rejections with normal roentgen findings, abnormal cardiac roentgen findings with normal clinical findings and the abnormal group where they both agree.

Table II

Calcifications: total 536.0 in 10,000 cases
Rejected because of too many or too large in 3.313 cases
Total 16.0 = 4.8 per 1,000 population

TABLE III

LUNG LESION OTHER THAN TUBERCULOSIS
TOTAL NO. = 13

	No. per 1,000 Population
Pneumoconiosis	0.1
Bronchiectasis	0.3
Tumor	0.1
Metastatic malignancy	0.1
Pleural thickening	0.5
Substernal thyroid	0.1
Atelectasis	0.1

TABLE IV

REINFECTION TUBERCULOSIS. TOTAL REJECTED 136

	No.	Percentage of All Tuberculosis Cases	Per 1,000 Population
A. Healed	65	47+	6.5
Active	71	52+	7.1
B. Previous history of tuberculosis	46	33+	4.6
No history	90	66+	9.0
C. Positive history	46 cases		
Active	20	14+	2.0
Healed	26	19+	2.6
D. No history	90 cases		
Active*	51	37	5.1
Healed	39	28	3.9

* 14 active cases had cavities; 1.4 cases with cavities per 1,000 population.

The healed cases, likewise, are of no immediate problem. The number that have healed never being aware of their disease is 50 per cent greater than those who have been treated.

What is of significance, from the public health standpoint and to the individual, are the 5 cases per 1,000 going about with active lung disease without symptoms, unaware of their illness. That this can be extensive is evident on some of the cases examined. Twenty-eight per cent of this group have cavities.

CONCLUSIONS

1. Roentgen examination offers the best present method of detecting the small minimal tuberculous lesions.

2. The 4×5 inch stereo film is the most satisfactory for chest surveys. It is more economical and easier to handle than the conventional single 14×17 inch film and has the same, if not better, diagnostic accuracy.

3. The incidence of reinfection tuberculosis in a cross section of healthy adult male population between the ages of twenty-one and thirty-five is between 1.2 and 1.35 per cent. Of this group over 50 per cent are active or have an arrested disease. Two-thirds of those with reinfection tuberculosis are not aware of having or having had the disease.

4. Widespread tuberculosis with cavitation can be present without symptoms.

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THE ROENTGENOLOGIC DIAGNOSIS OF DILATATIONS OF THE SPINAL CORD VEINS*

REPORT OF A CASE

By BERNARD S. EPSTEIN, M.D., *and* LEO M. DAVIDOFF, M.D.
BROOKLYN, NEW YORK

VENOUS dilatations of the spinal cord is an uncommon condition which is difficult to diagnose clinically. Routine roentgenographic examinations of the spine offer no help. In 1927 and 1929 two cases were reported in which iodized oil myelography revealed a peculiar distribution of droplets of oil over two or more vertebral segments.[3,7] These were the first instances in which the roentgenographic findings were important. Black and Faber[1] reported a case in which the appearance of a Froin syndrome, a Queckenstedt test changing from negative to positive after removal of spinal fluid from below the lesion and alterations in the distribution of iodized oil within the spinal canal as seen on myelograms was believed indicative of spinal venous dilatations. Buchanan and Walker[2] also noted a peculiar distribution of oil within the spinal canal in a patient five years old. They did not consider this appearance characteristic of any specific entity.

Intraspinal vascular dilatations may occur as true dilatations of the pial veins, as arterial or arteriovenous aneurysms or as hemangiomas. Because individual instances of arterial or arteriovenous aneurysms can be distinguished only with difficulty from true venous dilatations these two groups can be separated only on morphologic differences. They occur with approximately equal frequency and form 90 per cent of the cases reported.[4] The hemangiomas form a separate group and are neoplastic.

One of the two usual explanations offered for the presence of non-neoplastic venous dilatations is the existence of some interference in the spinal venous circulation which results in varix formation. This concept is supported by the findings recently reported by Hare and Everts.[5] They describe a patient who developed calcifications within the spinal canal after an injury. Twenty-five years later varices were found above the calcific area at operation, and they concluded that slowing of the venous circulation by pressure of the lime salt deposit had resulted in the formation of varices. The second explanation is the presence of congenital anomalies in the development of the veins resulting in angiomas.[8] The case we are reporting probably falls into the latter group.

The importance of the condition depends on the extent of the dilatations and the resultant increase in intraspinal pressure. Minute dilatations may exist without producing symptoms, such as have been mentioned by Kaydi[6] in patients who had no evidence of central nervous system disease.

The distribution of iodized oil within the spinal canal offers a roentgenologic approach to the diagnosis which is worthy of more detailed description. The dilated veins lie in the spinal canal surrounded by the cerebrospinal fluid. Depending on the degree of engorgement, various pressure points may be produced within the spinal cord and the circulation of the spinal fluid may be impeded. Inasmuch as the veins may on occasion be dilated and at other times collapsed, a constant roentgenographic picture should not be anticipated. If the fluid is displaced by the iodized oil, the varices dilated at the time show up as a pattern of negative serpentine shadows

* From the Radiologic Service of M. G. Wasch, M.D., and the Neurosurgical Service of L. M. Davidoff, M.D., The Jewish Hospital of Brooklyn.

because the oil cannot cover the dilated veins.

We are presenting a fifth case with roentgenographic findings. The diagnosis was established preoperatively by one of us (L. M. D.) on the basis of the myelograms.

REPORT OF CASE

J. S., male, aged forty-three, had noted pins and needles sensations over the right buttock and the right lower extremity for eleven years. The onset of the paresthesias was sudden, and the initial attack lasted two weeks and then disappeared spontaneously. Since then there had been frequent recurrences varying from a few minutes to several hours in duration and of varying degrees of pain. These episodes appeared without apparent cause and disappeared without sequelae. The patient had noted difficulty in starting and stopping his urinary stream for about ten years before admission. Five years ago cystoscopic examination and examination of the prostatic secretion were reported as normal.

The patient remained in relatively good health until one year ago. At that time he noted weakness of his right lower extremity and stumbled frequently, most often with his right foot. Two weeks before admission dull constant pain in the lower spinal region appeared, and one week later there was numbness without paresthesia of the right lower limb. The day before admission numbness appeared in the left foot. He had had three episodes of uncontrollable shaking of the right lower extremity during the five months before admission. Each episode lasted about five minutes.

Physical Examination. The patient was well developed and nourished. He walked with difficulty, his right leg was stiff and he shuffled his right foot along the ground. There was a positive Romberg sign, although he did not fall to any particular side. The motor power of the neck, upper extremities and trunk was good. There was weakness of both lower extremities, particularly in the right hamstring group. Moderate hypesthesia from the level of the seventh and eighth thoracic segments to the first lumbar segment anteriorly and posteriorly was present. Below the first lumbar segment the hypesthesia was less marked. The perception of vibration was absent from both lower extremities, and just perceptible at the anterior iliac spines. There was loss of position sense of the big toes. The finger-to-nose test was performed satisfactorily. The heel-to-knee test showed marked loss of position sense bilaterally. There was no dysdiadokokinesia.

Fig. 1. "Spot" roentgenogram taken under roentgenoscopic control demonstrating a large varix in the lower cervical region. The varix is outlined by the parallel serpentine distribution of the iodized oil. A smaller varix is seen in the mid-cervical and upper thoracic region.

Examination of the cranial nerves showed no evidence of abnormal responses. The Babinski reaction was doubtfully positive on both the right and left sides. The knee jerks, ankle jerks, biceps, triceps, radial and ulnar reflexes were intact. There was tenderness over the spine from the twelfth thoracic to the fourth lumbar

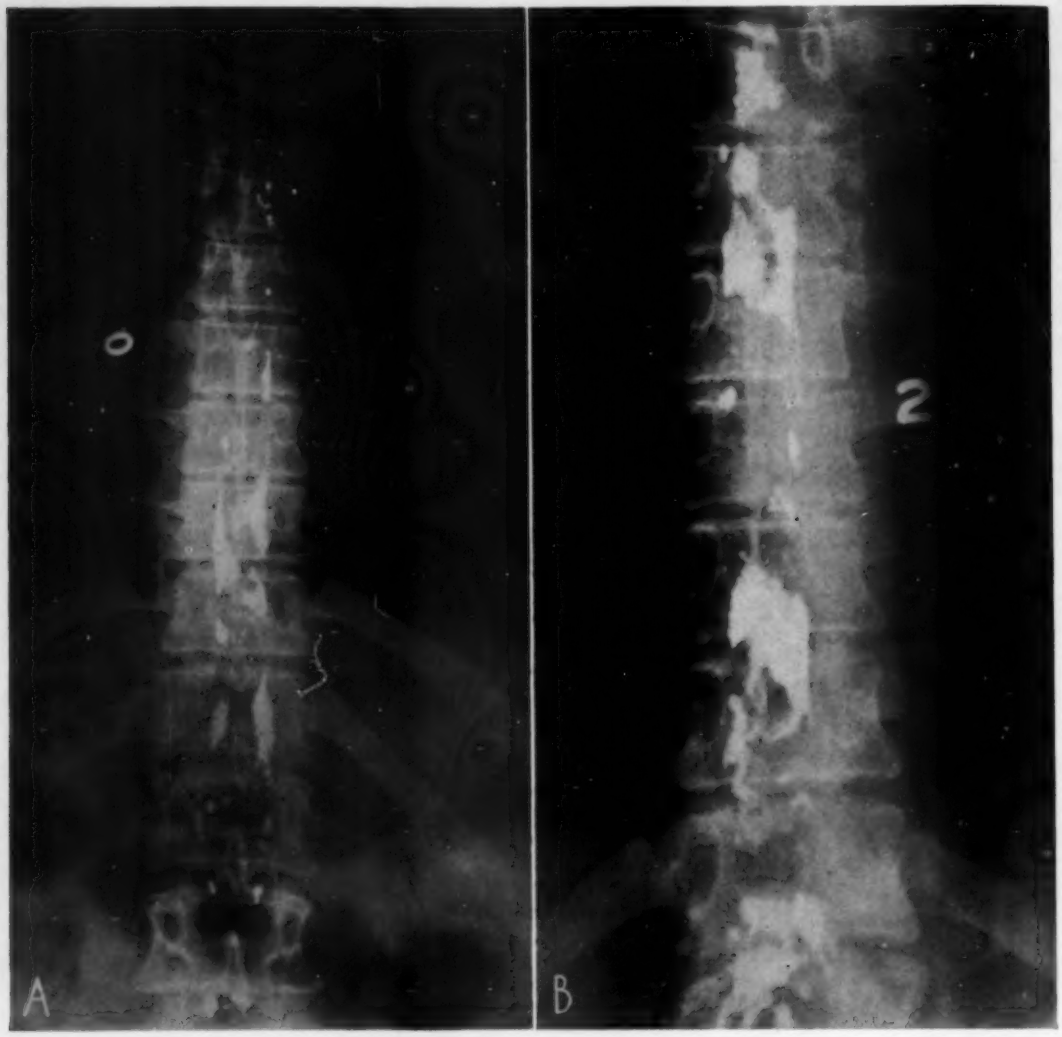

Fig. 2. *A*, "spot" roentgenogram showing varix at the level of the tenth, eleventh and twelfth thoracic vertebrae. *B*, roentgenogram taken three days later showing alteration in the distribution of the iodized oil. Another varix at the level of the seventh thoracic vertebra can be demonstrated.

vertebrae. The rectal sphincter tone was good. The abdominal reflexes were absent.

Spinal tap showed an initial pressure of 138 mm. of water, which fell to 84 mm. of water after the withdrawal of 10 cc. of fluid. There was no evidence of manometric block. The total protein was 120 mg. per 100 cc. Globulin was 2 plus. The Wassermann reaction was negative.

Direct roentgenographic examination of the spine showed no evidence of an osseous pathological condition. The measurement of the interpedicular spaces according to the Elsberg and Dyke curve was normal.

Examination of the spine after the introduction of 2.5 cc. of iodized oil showed no evidence of block. Roentgenoscopic inspection revealed free flow of oil from the caudal sac to the cervical region. Roentgenographic examination revealed the presence of numerous negative shadows with smooth, parallel sides. These were present in the lumbar, thoracic and cervical regions, and measured up to 1 cm. in width. The findings were interpreted as due to serpentine venous dilatations over the entire spinal cord.

A laminectomy exposing the seventh, eighth and ninth thoracic vertebrae was performed.

Incision of the dura revealed a thick vermiform varix about 5 mm. in diameter on the dorsal aspect of the cord extending cephalad and caudad beyond the limit of the operative field. The varix was bluish red, and as far as could be ascertained did not appear to be thrombosed at this particular site. The lesion was considered inoperable and the wound was closed in layers.

Following operation the patient was in continual severe pain. He died suddenly about two weeks later. Autopsy permission could not be obtained.

COMMENT

From a clinical point of view, the variation in the symptoms with exacerbations and marked remissions may be significant for this type of lesion since it probably indicates variations in the degree of vascular dilatation in the lesion. Another very important point is the considerable increase in total protein in the cerebrospinal fluid (120 mg. per 100 cc.) in the absence of a manometric block. This would suggest that transudation may occur through the thin-walled blood vessels which comprise the lesion.

We believe, as was true in our case, that the diagnosis can be made from lipiodol myelography, but that the above points in the clinical record may lead to a suspicion of the correct diagnosis before myelography is done.

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EXPERIENCES WITH ROENTGEN IRRADIATION FOLLOWING OPERATION ON BRAIN TUMORS*

By STUART N. ROWE, M.D., F.A.C.S., *and* HAROLD W. JACOX, M.D.
From the Landon Surgical Clinic and the Department of Radiation Therapy, Western Pennsylvania Hospital
PITTSBURGH, PENNSYLVANIA

THE treatment of patients suffering from gliomas of the brain is for the most part unsatisfactory and as depressing as is the treatment of rapidly growing neoplasms in other parts of the body. However, we have been impressed by the good palliative results often obtained in seemingly hopeless conditions by operation and subsequent irradiation, and have been prompted thereby to review our experience in this field. We have collected a group of cases of known cerebral gliomas (excluding pituitary neoplasms, metastatic tumors and meningiomas) and a group with strong presumptive evidence of such a lesion, with follow-up observation of at least one year of the patients who are living. The known tumors consisted of 8 glioblastomas (multiforme), 6 medulloblastomas, 5 astrocytomas, and 2 mixed gliomas. In 12 patients no tumor tissue could be obtained at operation. From the standpoint of location there was a wide diversity, essentially every area of the brain being represented with the exception of the occipital lobe. These 33 cases have not been considered adequate material for a statistical study, but we feel they indicate the trend of our clinical experience.

While it is the purpose of this paper to discuss therapy primarily, one or two remarks concerning diagnosis may be apropos. In several instances delay in establishing the diagnosis may have handicapped the treatment. The error usually resulted from the incorrect interpretation of an isolated symptom such as vomiting, generalized convulsions, or impaired vision. We have been impressed with the value of ventriculography and have employed it in two-thirds of these patients. Although its use appears to be a confession of weakness in neurological localization or diagnosis, we feel that the benefits derived are manifold. The ventriculogram permits a minimal-sized surgical exposure and to some extent indicates the depth of the lesion, and even if the tumor cannot be reached at operation the films provide a reasonable basis for diagnosis and localization. This last point may be very vital in deciding upon the use of radiation therapy and choice of fields if it is used. We have found postoperative ventriculograms much more difficult to carry out adequately and to interpret.

In the cases of verified tumor only one gross error of localization was made—the rather classic one of mistaking a tumor close to the third ventricle for a lesion in the posterior fossa. Fortunately, this patient survived the negative cerebellar exploration as well as a later ventriculogram and correctly placed surgical attack (see Case III).

The effects of operation alone were difficult to determine. The time interval between the surgery and irradiation was usually short—varying from ten days to two months with an average of three weeks—thus permitting estimation of immediate results only. On this basis, as far as could be judged, about half the patients were definitely benefited by surgical removal of the tumor or by decompression. Doubtless in an additional group some of the later improvement was related to operation as well as to irradiation, a point which will be considered below.

* Read before the American Academy of Neurological Surgery, San Francisco, California, Nov. 15, 1941, and the Pittsburgh Surgical Society, Jan. 16, 1942.

The technique of the roentgen therapy was not marked by startling innovations. Instead of adopting any fixed numerical maximum exposure, we aimed to irradiate each patient to the limit of his tolerance. Treatment with high voltage roentgen rays (200 kv. and 0.5 mm. copper filtration) was begun slowly in an effort to minimize the reaction—particularly elevation of intracranial pressure—but if the patient's general condition and the tolerance of the scalp would permit, rather large total amounts were given (up to 3,400 r, measured in air, to one portal and totals of 7,700 r divided among four portals). Usually exposures of 100 to 200 r were given daily except Sunday, for approximately three weeks. Subsequent series were administered chiefly when the beginning of a clinical decline indicated their need (unless the condition of the scalp demanded further delay), the shortest interval between series being four weeks. We have not used radiation therapy through the open wound.

Obviously numerous factors affect the results of roentgen treatment (location of the tumor, size of the tumor, age and general condition of the patient, etc.), but certainly the pathologic type of neoplasm is of primary importance.

The glioblastoma multiforme (or spongioblastoma multiforme) is perhaps the most discouraging type of cerebral tumor. Frequently the lesion is far advanced when seen by the neurosurgeon, usually its depth and extent make complete removal impossible, and even after block resection its tendency to recur is notorious. Here would seem to be an ideal field for roentgen therapy. However, we have encountered two difficulties: First, a number of our patients were so ill that the burden of large amounts of roentgen radiation could not be added. Even with preliminary decompression or partial removal, adequate therapy could not be tolerated by the patient and the general down-hill course could not be halted. In another group the tumor was apparently unaffected by irradiation and continued its rapid growth. In approximately half our patients the results were hampered by one or the other of these factors. In the remaining cases, particularly when most of the tumor could be removed and extensive irradiation tolerated, worthwhile prolongation of the patient's confortable and useful life occurred. Such a result is illustrated by the following case:

Case 1. L. M., white male, aged forty-five, was well until two years before admission when he suddenly experienced a fainting spell, followed by severe headache. A year before entrance the same thing happened again and this was followed by nausea and vomiting and occasional headaches. The headaches gradually became more severe and in the last nine months were localized to the left temporal region.

The patient was first studied by one of us (S.N.R.) in the Veterans' Administration Facility, Aspinwall, Pennsylvania, where the clinical picture was suggestive of an intracranial aneurysm with repeated subarachnoid hemorrhage.

When he was seen two months later neurological examination showed choked discs of about two diopters, complete loss of the temporal visual field on the right and slight cutting of the nasal field of the left eye, and a marked mixed aphasia. Ventriculograms disclosed a shift of the entire ventricular system to the right, and a defect in the temporal and parietal portions of the left lateral ventricle.

At operation (November 2, 1940) a large, infiltrating, partly necrotic tumor was almost totally removed from the posterior portion of the left temporal and anterior part of the left parietal lobes. Microscopic section showed a typical glioblastoma multiforme.

Eleven days postoperatively the patient received the first of a series of high voltage roentgen treatments to two portals, cross-firing the left temporoparietal region. Each portal received 2,100 r (measured in air) within a period of eighteen days at the rate of 200 r per day.

The patient made a steady recovery with complete disappearance of all symptoms and more than one year after operation remains in good condition. He has been working full time for the past six months.

Medulloblastomas are generally considered to be the most radiosensitive of the

gliomas,—indeed a preliminary trial of roentgen therapy has been advocated for clinically suspected tumors of this type. Fearing the development of fatal medullary compression we have not used such preoperative treatment. Despite their radiosensitivity the clinical response to irradiation was less than we anticipated in our series. The failures seem to result either from a tendency of the tumor to become radioresistant or the development of cord metastases which recurred in spite of intensive therapy. It may be argued that the latter difficulty ensues because the operative attack leads to seeding of the tumor down the spinal canal but in one instance in this series spinal metastasis occurred before operation. The following case is representative of our experience:

Case II. A. Z., male, aged seventeen, referred by Dr. S. B. Meyers, of Johnstown, Pennsylvania, had been troubled for about one year by dizziness upon bending over. Five months before entrance left-sided tinnitus, headaches and pain in the back of the neck followed by nausea and vomiting developed. These symptoms became steadily worse until admission.

Examination revealed only very slight bilateral signs of cerebellar dysfunction and bilateral papilledema of four dipoters. Routine roentgen examination of the skull showed prominent convolutional markings in the frontal and parietal regions, but no other abnormalities. Ventriculograms demonstrated enormous dilatation of the lateral and third ventricles with obstruction of the lower end of the aqueduct.

The usual suboccipital craniectomy revealed a soft reddish tumor in the left cerebellar hemisphere which also infiltrated the vermis and the floor of the fourth ventricle. Only a small portion of the tumor was removed for biopsy, the pathologic report being "protoplasmic astrocytoma."

Beginning ten days postoperatively the patient received 3,000 r (measured in air) in twenty days to a field 8 by 10 cm. in size directly over the cervico-occipital region, given at the rate of 100 to 200 r per day. He made an excellent recovery and was normal except for slightly impaired vision for three months when he returned complaining of numbness of the right leg and left chest, suggesting spinal cord involvement. During this admission 1,400 r to each of three long narrow portals over the entire spine was given and the symptoms disappeared. He returned in four months with signs and symptoms of cerebellar recurrence and 2,500 r was given to the suboccipital region and 600 r to each of three portals over the spine. The patient showed only slight response, however, and died two and one-half years from the date of onset or one and one-half years from the beginning of treatment.

In retrospect it is possible to see several defects in the handling of this patient. The biopsy was somewhat traumatized—which contributed to the erroneous pathologic diagnosis. Furthermore, when the spinal metastasis indicated the correct diagnosis of medulloblastoma, therapy was not given over the cerebrum. Although no clinical evidence of such a lesion existed, it is barely possible that intraventricular metastases may have been present. Nevertheless, the local recurrence of the tumor despite previous heavy irradiation emphasizes the terminal radioresistance of this tumor.

It is generally agreed that astrocytomas grow slowly, are radioresistant, and occasionally are amenable to complete surgical extirpation. On the basis of these beliefs irradiation is used relatively infrequently in combatting such tumors and our experience is limited to 5 patients, who for varying reasons received therapy. Two of these appeared to be benefited, and a summary of the record of one may be of interest.

Case III. P. G., female, aged six, one of a set of twins, referred by Dr. M. H. Weinberg, was in good health until September 1, 1939, when she began to have intermittent projectile vomiting, unsteadiness of gait and balance, impaired vision and urinary incontinence. These symptoms progressed during the four months before her admission. Examination showed the classical signs of a cerebellar tumor of the left hemisphere with no evidence of brain stem involvement.

Ventricular estimation indicated an internal hydrocephalus. Operation (January 4, 1940)

using a cerebellar approach did not reveal the tumor. Subsequently a ventriculogram disclosed a defect in the third ventricle. Through a right transfrontal approach (January 12, 1940) approximately one-third of an infiltrating tumor near the anterior part of the third ventricle was removed. Microscopically the tumor was an astrocytoma.

The patient had a very stormy and slow convalescence and remained in a state of decerebrate rigidity for weeks. Nevertheless, high voltage roentgen therapy was started seventeen days after the second operation and a total of 1,800 r (measured in air) was given to an anterior frontal and to a right and left temporal portal in twenty days. The child began to improve slowly and a year later was essentially symptom-free with the exception of a slight left hemiparesis, impaired vision, and occasional petit mal attacks. Because of the epilepsy 1,800 r was given to each of three portals exactly as before. Again improvement occurred and has been maintained for two years since the first operation.

Obviously this is a slowly growing neoplasm; however, it reached a point of producing nearly complete blindness and high intracranial pressure four months after symptoms began, whereas the child's present condition is reasonably good two years after treatment was instituted.

An unusual instance of a mixed glioma is worthy of mention. Definite evidence of extensive necrosis of the tumor and great decrease in the vascularity of the overlying tissues were found at operation following irradiation.

Fig. 1. Case iv. Roentgenogram of skull showing right frontal bone destruction, intracerebral calcification, erosion and enlargement of the sella turcica. The tumor proved to be a large mixed glioma.

Fig. 2. Case iv. Posteroanterior projection showing peculiar bone destruction in the right frontal region and increased density in the right orbital cavity.

Case iv. M. C., male, aged thirty-three, laborer, referred by Dr. R. B. Meyers, of Johnstown, Pennsylvania, noticed flashes streaking across his field of vision in November, 1936. He also had involuntary shaking of his right leg and foot. Four months later his vision began to dim gradually and this progressed almost to blindness in five months. A month before hospitalization the right eye began to protrude.

Upon admission in October, 1937, the most striking finding was the marked proptosis of the right eye. There were also clonic contractions of the right lower extremity. Roentgen examination of the skull showed erosion of the posterior clinoid processes and floor of the sella. There were small, irregular areas of bone destruction in the right frontal, parietal, and occipital regions, increased density in the right orbit, and right frontal calcification (Fig. 1 and 2). On October 20, 1937, a right subtemporal decompression was performed. Biopsy of the bone (November 11, 1937) adjoining one of the right frontal defects showed nothing abnormal. At both operations extreme vascularity of all tissues was noted.

Beginning one month postoperatively he received a total of 1,200 r to each of three portals in twelve days, cross-firing the anterior half of the skull. There was definite improvement in

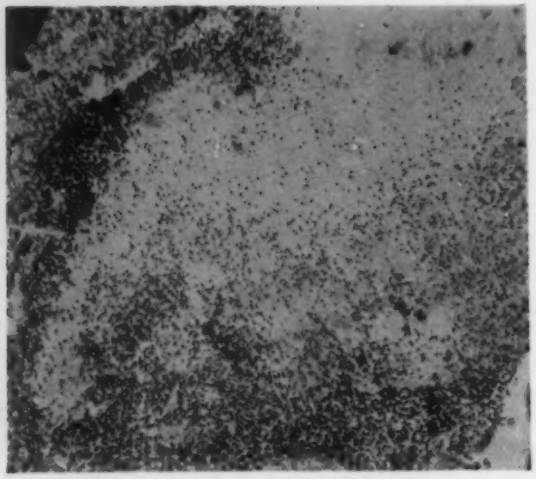

Fig. 3. Case iv. Photomicrograph of mixed glioma following irradiation. The border of a large area of necrosis is seen in this field. Hematoxylin and eosin stain; low power.

the proptosis and later 1,800 r was given to each of the same three areas in thirty-one days. Again there was improvement, but the patient developed a cerebrospinal rhinorrhea.

On November 25, 1938 a right transfrontal craniotomy was performed and a degenerated, necrotic tumor 6 or 7 cm. in diameter, occupying the greater part of the right anterior cranial fossa, was removed. Microscopically this proved to be an interesting mixed glioma, for the most part resembling astrocytoma but showing areas of definite glioblastoma multiforme (Fig. 3). This type of tumor has recently been discussed by Munro, Edwards and Russell.[3]

Ten days postoperatively a third series of roentgen treatments consisting of 1,700 r to each of four portals was given in nineteen days. Again he was improved for about six months when the proptosis became worse and the vision almost nil. A final course of 2,700 r was given to one large anterior frontal portal in ten days. He was fairly comfortable up to his death at home three years and four months after the onset of symptoms and nearly two and one-half years after the first hospitalization.

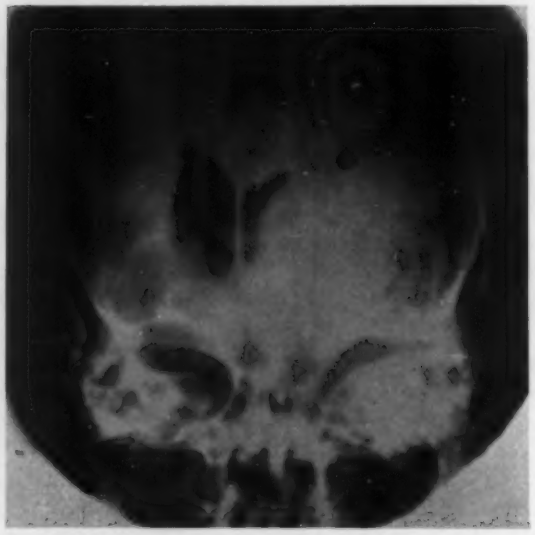

Fig. 4. Case v. Ventriculogram showing displacement of the entire ventricular system to the right and dilatation of the right lateral ventricle.

Fig. 5. Case v. In the lateral ventriculogram the dilated right lateral ventricle and the absence of filling of the parietotemporal portions of the left lateral ventricle are illustrated.

There remains the group of patients in whom no tumor tissue was obtained at operation. Should one irradiate the unverified tumor? Certainly the decision must be made in each case on its own merits. Where there is a gross error of diagnosis or localization, the mistake usually becomes apparent soon after the surgical attack and obviously irradiation should not be undertaken. But when the failure of verification is due to the deep situation of the tumor and strong clinical and ventriculographic evidence of its presence are at hand, roentgen therapy has proved very helpful in our experience. In more than half of our group of 12 cases of this type marked clinical improvement

has been obtained. One very striking example indicates the problems involved as well as the results of therapy.

Case v. M. N., white female, aged twenty-one, referred by Dr. Martin, of Duquesne, Pennsylvania, came to the Western Pennsylvania Hospital in July, 1938, for relief of convulsions which she had had for three years. The convulsions were jacksonian in type on the right and increasing in frequency. For three months she had noticed blurring of vision in the left eye.

Neurological examination showed only bilateral papilledema and slight reduction of visual acuity. The patient had a linear area of left frontal scleroderma (of long standing) which extended across the forehead to the nose.

Routine roentgenograms of the skull showed evidence of considerable increase in intracranial pressure. Ventriculograms showed moderate enlargement of the right lateral ventricle and a shift of both lateral ventricles and the third ventricle to the right (Fig. 4 and 5).

At a left parietotemporal craniotomy on August 2, 1938, the brain was under great pressure, and no tumor could be seen or reached with a brain cannula. Nine days later a second attempt was made through an incision in the left temporal lobe but no neoplasm was found.

Two months later the decompression was bulging and a series of high voltage roentgen treatments was given over both sides of the head. Two thousand roentgens (measured in air) was given to each temporoparietal portal in fifteen days. The bulging disappeared two months after completion of the treatments and the patient became almost entirely normal.

Seventeen months later the patient developed aphasia, weakness and tremors of the right upper extremity and occasional short attacks of unconsciousness. Fifteen hundred roentgens was applied to three smaller portals, but otherwise exactly as before.

During the first month after the second series of treatments the patient suffered one jacksonian attack accompanied by aphasia and pain in the left parietal region. Another ventriculographic study showed the left lateral ventricle obstructed and pushed upward and outward in its posterior third. The third ventricle could not be seen. A third left parietotemporal craniotomy failed to reveal the tumor, though a transcortical incision was carried to a depth of 5 cm.

When seen six months after the second series of roentgen treatments the patient was in fair condition and was troubled only by moderate motor aphasia. At present she lives at her parents' home where she does much of the housework. She has had brain tumor symptoms for a total of six years, and has been under treatment over three years.

DISCUSSION

What proof is there that high voltage irradiation has any effect on most gliomas? The natural tendency is to attempt to answer the question on the basis of histologic sections before and after irradiation. It is obviously difficult to obtain tissue for post-irradiation examination in many cases. Furthermore there are several possible sources of error in this method: (1) changes in a tumor which are presumably the result of roentgen irradiation can be demonstrated histopathologically when the patient has shown little if any corresponding clinical improvement; (2) all the histologic changes which iradiation produces within a glioma may also occur spontaneously; (3) varying areas within the same tumor may present widely different histopathologic pictures. The shortcomings of this method have been recognized by others.[1,2,4]

The only other way of evaluating the results of roentgen irradiation is on the basis of the clinical course. This, too, has its pitfalls. It is difficult to separate the effects of operation from the effects of irradiation, or vice versa. Although a fairly accurate standard of life expectancy for a given type of glioma has been set up, it is practically impossible to predict the natural course of the disease for a given patient, in whom the duration, extent and location of the lesion cannot be sharply defined.

Nevertheless, we feel that in some cases it is possible to demonstrate clear-cut evidence of clinical improvement due to irradiation and believe that if reasonable caution is exercised, this method offers a satisfactory means of evaluating the therapy. Occasionally a false impression of the effectiveness of therapy might be

given by a slowly growing type of tumor. Because of this we have emphasized the preoperative duration of symptoms in discussing the postoperative and post-irradiation result in each case. Again late improvement may sometimes be the result of surgical treatment rather than of roentgen therapy. However, in several patients the response to operation was so slight and improvement following roentgen irradiation so definite that there could be little question of the effectiveness of the latter. In addition, a number of patients showed a definite response to irradiation at a stage when their gain from previous surgical or roentgen therapy was rapidly waning. Cases III and V illustrate this point very well.

In conclusion, we do not wish to leave the impression from the discussion or illustrative cases that we regard roentgen therapy as a panacea in the management of gliomas. As has already been stated, approximately half our cases followed a rapid down-hill course. However, the number of patients in the remaining group who obtained substantial prolongation of useful life as a result of operation and irradiation seems to justify the continued use of these methods even in cases of an apparently hopeless character.

Doubtless the accumulation of additional clinical and pathologic studies will eventually enable more accurate prognosis as to the results of roentgen therapy in gliomas, or lead to discovery of other more effective methods of treatment.

SUMMARY

1. The best results of combined surgical and roentgen therapy seem to be obtained when most of the tumor can be removed and intensive irradiation given without dangerously increasing the intracranial pressure.

2. There are frequent exceptions to the usually accepted rules as to the radiosensitivity of various types of glioma.

3. In dealing with brain tumors which are inaccessible surgically, decompression and irradiation may occasionally produce prolonged benefit.

4. Approximately half the patients in this series died within one year regardless of surgical or roentgen treatment. However, at the present time it is impossible to determine before treatment is begun which patients will fall into this hopeless group and which may be definitely benefited by treatment.

5. We believe that one is rarely justified in refusing operation or roentgen therapy or both even to the patient who presumably has an advanced, highly malignant, or deeply situated brain tumor.

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CANCER OF THE UTERUS

RESULTS OF THE PRESENT METHOD OF RADIUM THERAPY AS INFLUENCED BY STAGE AND GRADE OF THE LESION*

By HARRY H. BOWING, M.D., *and* ROBERT E. FRICKE, M.D.
Section on Therapeutic Radiology, Mayo Clinic
ROCHESTER, MINNESOTA

ALL of us are interested in the end-results attainable by carefully planned treatment of cancer of the uterus.

Prognosis is an important feature in the treatment of cancer. Although the patient should not be demoralized by too much information regarding the gravity of her condition and its probable outcome, the relatives and the referring physician are entitled to all the information at the radiologist's disposal.

THE PROBLEM IN CANCER OF THE UTERUS

Cancer of the uterus presents the problem of two dissimilar types of malignant lesion distinguished according to location: cancer of the cervix and cancer of the fundus of the uterus. The radiologist is forced to treat these two dissimilar lesions very differently. Because cancer of the cervix is accessible, in much of its extent, to inspection and careful palpation, the stage or extent of the lesion can be gauged with some degree of accuracy and, furthermore, the rate of response to radium treatment can be judged. Hence, in our opinion radium therapists should apply an individualized form of treatment to cancer of the cervix, whereas this is not possible with cancer of the fundus.

In the case of cancer of the fundus, we are trying to treat an invisible lesion. None of the neoplasm ordinarily can be seen, and the stage or extent can be only approximately judged by palpation and very limited inspection. The rate of response to treatment cannot possibly be determined. Hence, in dealing with an invisible lesion whose extent or stage is poorly defined, a rather standardized method of treatment must be employed.

Hence, there are two differing methods of treatment of these two forms of cancer. The results of radium therapy in cancer of the cervix do not approximate the surgical results as is the case of cancer of the uterine fundus, at least in our experience. We will attempt to show this in our present study.

We know that the stage or extent of the lesion is the most important single prognostic factor. In recent years a very important contribution has been made by the pathologist as an additional guide for the surgeon and the radium therapist. This additional prognostic guide is the microscopic grade of the lesion, known as "Broders' index."

STUDIES IN CANCER IN OTHER SITUATIONS

Cancer of the Stomach. The importance of both stage or extent and of the microscopic grade of cancer in prognosis is well illustrated by a study of surgical results. A study of the excised surgical specimen yields accurate information regarding the stage of a malignant lesion. In a recent work Dochat applied Dukes' method of typing cancer of the rectum to gastric cancer in an analysis of survival after surgical excision of the cancer. Dukes' typing was modified to include four types: in A, the cancer was confined to the gastric mucosa; in B_1 was included invasion of muscle, but not serosal involvement; in B_2, there was muscular and serosal involvement, and in Type C, involvement of regional lymphatic vessels and lymph nodes and even distant metastasis.

* Presented at the Twenty-seventh Annual Meeting, American Radium Society, Atlantic City, N. J., June 8–9, 1942.

TABLE I

CARCINOMA OF THE STOMACH: FIVE YEAR SURVIVAL RATE, COMPUTED ACCORDING TO DUKES' TYPE*

Lesion, Type	Patients			
	Traced	Per cent†	Alive 5 years after leaving hospital	
			Number	Per cent
A	20	1.9	20	100
B_1	113	10.8	69	61.0
B_2	294	28.0	130	44.2
C	618	59.3	95	15.3

* From: Dochat, G. R. A prognostic comparison of serosal and nodal spread in carcinoma of the stomach, with a classification into Dukes' types. Thesis, University of Minnesota Graduate School, 1941, p. 24.
† Of number traced.

Broders' microscopic grading of the malignant lesion also was utilized. One thousand two hundred and fifty-one cases of gastric cancer were studied. There were 200 operative or postoperative deaths; 30 per cent of the patients were living five years postoperatively. Results, computed according to stage, or Dukes' typing, are seen in Table I. When Broders' grading was employed the usual prognostic pattern was obtained. Results appear in Table II.

Dochat found that the best prognostic guide was a correlation of Dukes' and Broders' methods; that is, combination of the stage and grade. The microscopic grade is extremely valuable, but the value is enhanced by a combination with the extent or stage of the lesion. As Dochat pointed out, in cancer of the stomach a Type B_2, Grade 4 lesion is accompanied by a better prognosis than is a Type C, Grade 2 lesion for instance.

Cancer of the Rectum. In Dukes' original work rectal cancer was typed according to extent and this was correlated with postoperative survival. Three types were used: in A, the cancer was confined to the rectal wall; in B the cancer had penetrated to the serosa; and in C the regional lymph nodes and lymphatic vessels were involved. Duke found that by studying both the extent and the microscopic grade the prognosis was simplified and was much more nearly accurate. Studies have shown that patients who have rectal cancer of Type A of any grade, with the exception of Grade 4, have a fairly good prospect of a five year survival.

CANCER OF THE UTERINE CERVIX

This lesion is a cancer sufficiently accessible for fairly accurate preliminary study. In a case of the medullary type, part of the neoplasm is visible and palpable, permitting rather definite delineation of the stage or extent; biopsy furnishes the microscopic grade. The rate of response of the cancer to radium treatment can be directly observed from day to day. Radium therapy hence can be and usually is individualized. Space will not permit a detailed discussion herein of the various radium therapeutic techniques and methods of individualization employed by others.[6] Briefly, our early experience demonstrated to one of us (Bowing) the value of individual treatment in meeting the therapeutic demands of the patient under treatment. The knee-chest position was the most important single part of the procedure, for it permitted the radium therapist to observe the gross appearance of the lesion, the identity of anatomic landmarks to facilitate distribution of the dose and the rate of response ob-

TABLE II

CARCINOMA OF THE STOMACH: FIVE YEAR SURVIVAL RATE, COMPUTED ACCORDING TO BRODERS' GRADES*

Lesion, Grade	Patients			
	Traced, number	Per cent†	Alive 5 years after leaving hospital	
			Number	Per cent†
1	4	0.3	4	100
2	237	22.7	107	45.5
3	408	38.6	120	29.4
4	402	38.4	83	20.6

* From: Dochat, G. R. A prognostic comparison of serosal and nodal spread in carcinoma of the stomach, with a classification into Dukes' types. Thesis, University of Minnesota Graduate School, 1941, p. 24.
† Of number traced.

tained from the applications of radium and the local cleansing procedures employed, and the like. The radium technique we employ may be referred to as a broken-dose, intensive method. The filters, treatment time, distribution of the dose throughout the involved area, and the time interval between treatments are so selected as to meet the individual requirements of the patient. At the end of a complete course of radium therapy, which usually requires about three weeks for a patient with a Stage III cancer of the uterine cervix, a supplemental course of roentgen therapy is administered. A follow-up examination carried out every three months for the first year is recommended. We have found the method[3] very satisfactory in that it allows a very wide range of individualization.

From 1915 to 1929, inclusive, we found that 8.7 per cent of the patients referred for radium therapy had lesions of Stage I and Stage II, and that 91.3 per cent had lesions of Stages III and IV based on the League of Nations classification.[5]

Our five year "cures" obtained with radium treatment and supplementary roentgen therapy, based on 1,491 patients,[2] according to stage, were as follows: Stage I, 69.2 per cent; Stage II, 60.2 per cent; Stage III, 29.7 per cent and Stage IV, 6.5 per cent.

Surgical operation is confined in selected cases to lesions of Stages I and II. The rate for five year "cure" of cancer of the cervix by total abdominal hysterectomy with irradiation, based on 165 patients seen from 1910 to 1938, inclusive, was 57.1 per cent of the traced patients.[7]

In this study we considered surgical methods as constituting a rather standardized procedure. Excellent radical operative procedures have been evolved which are employed by skilled surgeons everywhere. As Masson[7] has said, "The type of surgical procedure indicated for carcinoma of the uterus will probably never be improved."

Next in importance to the stage or extent of the lesion is the microscopic grade of the cancer, which has been recognized to be in the main of surgical prognostic importance in that patients who have a low grade lesion do well, whereas patients who have a high grade lesion do poorly, after surgical intervention. In our own experience, of patients referred for radium therapy of cancer of the cervix, only 16 per cent had lesions of Grades 1 and 2, and 84 per cent had lesions of Grades 3 and 4.

Table III

RESULTS OF RADIATION THERAPY FOR CARCINOMA OF THE UTERINE CERVIX, BASED ON THE GRADE OF MALIGNANT CHANGE

Lesion, Grade	Patients			
	Treated	Traced	Lived 5 years or more after treatment	
			Number	Per cent*
1	5	5	2	40.0
2	135	122	40	32.8
3	407	362	125	34.5
4	336	307	105	34.2
Total	883	796†	272	34.2

* Percentage of traced patients.
† 90.7 per cent traced; total, 1,491 patients.

With the individualized radium therapy employed, and on the basis of a survival of five years, results of treatment of carcinoma of the cervix show that lesions of Grades 3 and 4 are no more fatal than are lesions of Grades 1 and 2. Patients who had Grade 1 lesions were too few to consider, but 135 patients with Grade 2 lesions were followed, and of this number 40 patients, or 32.8 per cent, lived five or more years. There were 407 patients with Grade 3 lesions, and of these 125, or 34.5 per cent, lived five years or more. There were 336 patients with Grade 4 lesions, and of these 105, or 34.2 per cent, survived five years or more. The five year "cure" rate computed according to grade of lesion is shown in Table III.[1] It is seen that the rate is, roughly, the same in all grades, but that only 5 patients with lesions of Grade 1 were treated.

When patients treated by surgery as well as by irradiation are added (referring again to Masson's study of 1939, embracing ex-

Table IV

CARCINOMA OF THE CERVIX: SURGICAL AND IRRADIATION RESULTS, 1910–1939*

Malignancy, Grade	Patients Traced	Per Cent of 5 Year Cures
1	5	60.0
2	190	41.1
3	678	37.9
4	511	33.7

* Adapted from Masson.[7]

perience from 1910 to 1938), the five year survival rates computed according to grade evolve as shown in Table IV.[7] Patients who had Grade 1 lesions obtained the best results and those who had Grade 4 lesions obtained the poorest results Results are calculated on the basis of a selected group of patients and yet may show the influence of standard treatment procedures. Evidently, in cases of cancer of the uterine cervix, we lack sufficient numbers of patients in certain grade and stage groups for satisfactory studies of correlation of microscopic grade with stage, as shown in Table V. For example, there were only 10 Stage 1 cases and 5 Grade 1 cases (Table V) out of the total of 883 lesions previously recorded in Table III. There seemed, however, to be sufficient distribution of grade in Stage III lesions for correlation purposes, although again the Grade 1 lesions are too few for purposes of such a consideration (Table V). For correlation determinations we selected Stage III lesions of Grades 2, 3 and 4 from Table V for computation of survival rates of five or more years, and again the survival rate in each grade in this group rather equal: 35.0, 34.1 and 35.1 per cent, respectively (Table VI). We submit that these data, based on a limited number of cases, probably indicate the influence of a tedious individualized radium therapy technique, designed to meet the requirements

Table V

CARCINOMA OF THE UTERINE CERVIX TREATED BY IRRADIATION ALONE, 1915–1929 DISTRIBUTION ACCORDING TO STAGE AND GRADE OF MALIGNANCY

Stage	Grade				Total
	1	2	3	4	
I	—	—	7	3	10
II	1	11	30	28	70
III	4	109	322	254	689
IV	—	15	48	51	114
Total	5	135	407	336	883

Table VI

CARCINOMA OF THE UTERINE CERVIX TREATED BY IRRADIATION ALONE: FIVE YEAR SURVIVAL RATES ACCORDING TO STAGE AND GRADE, 1915–1929

Stage of Lesion	Microscopic Grade of Lesion (Broders' Index)											
	2				3				4			
	Patients				Patients				Patients			
	Total	Traced	Alive 5 years or more after treatment		Total	Traced	Alive 5 years or more after treatment		Total	Traced	Alive 5 years or more after treatment	
			Number	Per cent*			Number	Per cent*			Number	Per cent*
III	109	100	35	35.0	322	287	98	34.1	254	231	81	35.1
IV	—	—	—	—	48	41	3	7.3	51	47	4	8.5

* Of traced patients.

of the patient being treated, on the results to be obtained.

CANCER OF THE UTERINE FUNDUS

Cancer of the uterine fundus presents a great irradiation therapeutic problem. It is considered to be a less malignant neoplasm than cancer of the cervix; the rate of growth appears to be slower and the tendency to metastasize develops later.

If the diagnosis can be established while the lesion still appears to be confined within the mucosa of the uterine walls, a less radical operation than is required for cancer of the cervix, and generally accomplished with less risk, usually is curative. However, when the disease is advanced and has infiltrated surrounding tissues or metastasized to other organs, worth-while palliation or even cure can be secured by radiation therapy alone.

Cancer of the uterine fundus is a hidden lesion, not accessible to inspection and less revealing on palpation than is cancer of the uterine cervix, so that the stage of the lesion is more difficult to evaluate. The diagnosis must always be established by study of the tissue obtained by curettage. The stage or extent can be determined only by the results of pelvic, general and special examinations. We have classified the lesion into four stages to correspond to the classic four stages of cancer of the cervix. Briefly, in Stage I the neoplasm apparently is superficial, the uterus is normal in size and is freely movable. In Stage II, the lesion has increased and involves the muscular wall; the uterus may be enlarged, although it is still movable. In Stage III is revealed extension beyond the uterine walls to neighboring tissues, with beginning fixation. In Stage IV, "frozen pelvis" has occurred, often with involvement of the bladder or rectum, or both, or a small primary lesion has metastasized to distant organs.

Results of surgical and radiation therapy vary according to the stage or extent, and also the microscopic grade, of the lesion. As Sackett[8] has reported, panhysterectomy with supportive irradiation accomplishes a five year cure in from 55 to 75 per cent of cases in this country; radiation therapy alone, in cases in which the disease is more extensive (precluding surgery) achieves a five year survival for from 25 to 50 per cent of the patients treated.

Masson,[7] in reviewing data concerning patients treated from 1910 to 1938, inclusive, at the Mayo Clinic, showed that in respect to five year survival rates total abdominal hysterectomy with and without irradiation yielded almost similar results: 67.5 per cent and 66.6 per cent, respectively (Table VII).

In later years, more amenable lesions have been treated by irradiation in preference to surgery. Better diagnostic methods have revealed lesions in earlier chronologic stages. But, since cancer of the uterine fundus is mainly a postmenopausal condition which afflicts women of a later age group, many unrelated degenerative diseases often complicate the picture and increase the operative risk. In a later review of patients treated by radium alone from 1925 to 1935, inclusive, our five year sur-

TABLE VII

CARCINOMA OF THE UTERINE FUNDUS: SURVIVAL RATES ACCORDING TO OPERATION AND IRRADIATION, 1910–1938*

Treatment	Treated	Died in Hospital, Per Cent	Traced	"Cured" 5 Years, Per Cent
Total abdominal hysterectomy with irradiation	194	1.0	191	67.5
Total abdominal hysterectomy without irradiation	306	8.5	296	66.6
Irradiation without hysterectomy	230	0.9	227	26.9

* Adapted from Masson.[7]

vival rate was seen to have increased to 39 per cent.[4] Practically a third of all patients seen at the Mayo Clinic with carcinoma of the uterine fundus have been referred for irradiation alone at this particular age period because of the extent of the lesion and the presence of associated degenerative diseases. Our five year survival rate has been influenced by the stage of the lesion,

Table VIII

CARCINOMA OF THE UTERINE FUNDUS: RESULTS WITH RADIUM THERAPY

Lesion, Stage	Patients Traced	Five Year Cures, Per Cent
I	15	93.0
II	29	52.0
III	32	34.0
IV	33	6.0

as is shown in Table VIII. The best results were obtained for those who had Stage I lesions; for them the five year survival rate was 93 per cent. The poorest results were obtained for those who had Stage IV lesions; for them the five year survival rate was only 6 per cent.

Results of this study showed clearly that determination of stage or extent of the neoplasm before treatment, although much more difficult in these cases, was accurate for prognostic purposes. Radium treatment was not individualized, but consisted of what may be considered standardized general irradiation along the entire length of the uterine canal achieved by tandems and single radium tubes, the number of tandems employed depending on the depth of the uterine cavity.

Table IX

CARCINOMA OF THE UTERINE FUNDUS TREATED WITH RADIUM

Grade	Patients Traced	Per Cent of 5 Year Cures
1	19	79.0
2	42	33.0
3	16	25.0
4	17	12.0
Not graded	15	47.0
Total	109	39.0

Results computed according to the microscopic grade of the lesion were surprising, from the standpoint of the radium therapist. Whereas, in cancer of the uterine cervix a lesion of Grade 4 was no more fatal than a lesion of Grade 2 (Table VI), high grade carcinomas of the uterine fundus were definitely more dangerous. Patients who had low grade cancer, considered by many as "radioresistant," did very well (Table IX).

SUMMARY

Brilliant improvement in surgical technique has developed the radical operations for cancer of the uterine fundus and for early cancer of the cervix to a high degree of efficiency. Results in well selected cases are excellent, and the operative procedures have become standardized in the hands of leading surgeons everywhere. The value of the present surgical technique has been proved and it is likely that no changes in the surgical approach will ensue.

In this study no new data have been presented, but we are submitting a conception or perhaps a "philosophy of treatment," which we have held for a long time. It seems very evident that to careful radium therapists the treatment of cancer of the uterine cervix is an individualized scheme. Not only do different clinics have varying methods of treatment, but the same radiologist will alter his method of attack on different lesions, because the lesions vary greatly and also because the rate of response to treatment probably differs with the amount of defensive factors of the patient's tissues against cancer. It is well known that radium can be used as cautery, or, if differently applied, will exert not a caustic but a healing effect, to which the reactions of the normal tissue greatly contribute. The latter effect is the most desirable in that it maintains to the highest degree possible the normal integrity of the

tissues in and near the involved malignant field.

Cancer of the uterine fundus presents the problem of a hidden lesion which is inaccessible to accurate estimation of its extent. Herein, to date, radium treatment has been rather standardized, consisting of homogeneous irradiation along the entire length of the uterine canal. Even though the percentage of "cures" or "arrests" secured with radium treatment alone has been encouraging, radiologists have put forth every effort to individualize the treatment. Heyman's multiple tube technique, the Schmitz Y-shaped applicator and the Friedman hysterostat are specific instances of this effort. This is encouraging, although in view of the nature of carcinoma of the uterine fundus these efforts will probably always be limited.

Radium treatment of cancer of the uterine fundus yields encouraging results, and in the course of time further advances in technique may succeed in creating a more flexible, less standardized program of treatment and may produce even superior results, comparable to those achieved by radium therapy in cancer of the uterine cervix.

CONCLUSIONS

1. The extent of the primary malignant lesion of the uterus is the most valuable prognostic factor.

2. The grade of malignant change (Broders' index) is a very valuable prognostic determination when more standardized surgical and radium therapeutic techniques are employed. This observation does not seem to be entirely true when individualized radium therapy is employed in cancer of the uterine cervix.

3. Evidently, the most individualized radium therapy designed to meet the demands of the patient under treatment for cancer of the uterus will give the best result.*

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* For discussion see page 515.

THE ELIMINATION OF IRRADIATION INJURIES IN THE TREATMENT OF CANCER OF THE CERVIX*

By CHARLES L. MARTIN, E.E., M.D., F.A.C.R.
DALLAS, TEXAS

RADIUM has been used successfully in the treatment of cancer of the cervix uteri for about thirty years, and the combined use of radium and roentgen radiation became popular a little more than twenty-five years ago. A variety of practical radium techniques was perfected early but when it was found that the more distant extensions of the disease could not be controlled with radium applied by the vaginal route, the evolution of a series of ingenious plans for increasing the irradiation effect of the periphery of the pelvis began. The advent of each new more powerful source of external irradiation has stimulated a renewed attack on the problem, and rightly so, since the total survival rate in large groups of unselected cases is still disappointing. This paper is written with no thought of discouraging those who are striving to perfect methods of treatment, but rather in an effort to stress the importance of the increased morbidity which has accompanied many of the new procedures. The tolerance of the normal structures always has been, and always will be, the limiting factor governing the use of radiant energy in the pelvis and it seems evident, as Miller and Folsome[17] have pointed out, that the most acceptable technique of the future will be the one which produces the largest number of good results with the lowest morbidity.

Our interest in this subject dates back to 1922, when several severe rectal reactions were observed following the use of vaginal radium. Soon afterwards, with the assistance of Dr. Fred T. Rogers, a series of observations was carried out on the effect of various doses of roentgen rays applied directly to exposed loops of small intestine in dogs. Unfortunately, no ionization measurements could be made at that time, and the changes in the dog's skin were used as a dosage indicator. This was not very satisfactory because the dog erythema dose was found to be much larger than the human erythema dose, but a series of changes closely paralleling those seen in treated patients were produced.

In 1923 it was shown[12] that the threshold erythema dose for the dog produced contraction of the wall of the intestine with a complete destruction of the mucosa, while the human erythema dose, as it was used clinically at that time, produced no visible changes in the intestine. Since the low voltage apparatus used for these experiments was discarded long ago, it is impossible to express the doses used in terms of roentgens, but by indirect computation it has been estimated that the dog erythema dose used in this work lies between 3 and 4 human T.E.D. If these figures be correct, this early work indicates that irreparable damage of the dog's intestine is produced by the administration of such a dose given continuously over a short period of time. Physical data indicate that the human rectum is capable of withstanding larger total doses with the accepted plans of therapy but no accurate measure of rectal tolerance under such conditions is available to me.

In 1924 an attempt[13] was made to study the end stages of the reaction produced by the application of the dog erythema dose to a single loop of intestine. In some instances the dogs developed a cachexia, accompanied by a severe diarrhea, from which they succumbed in about two months. In other instances they recovered from the primary reaction, but died in five or six months from obstruction, produced by a marked fibrosis and contracture of the irradiated segment.

* Presented at the Twenty-seventh Annual Meeting, American Radium Society, Atlantic City, N. J., June 8–9, 1942.

Patients having similar changes in the rectum following radium applications to the cervix were described by Benthin[2] in 1923, and Jeanneney and Wangermez[10] in 1929, and in 1930 Buie and Malmgren[3] reported 65 such cases observed at the Mayo Clinic. It is interesting to note that these latter authors stated that rectal damage following radium therapy was a justifiable complication. In 1932 Pemberton[18] described 7 rectal strictures, 3 sigmoid lesions and 1 case of ulceration of the ileum, and in 1935 Jones[11] reported 8 cases of stricture of the sigmoid and ileum severe enough to produce obstruction. In a personal communication he states that he has observed 10 additional cases since his paper was published.

Some have contended that the use of a prolonged divided dose roentgen-ray technique accounts for many of the rectal complications, but Healy and Frazell[8] found 9 rectal strictures in a group of 551 patients treated before the prolonged roentgen-ray procedure was adopted at the Memorial Hospital. Todd,[23] in reporting a series of almost 50 cases of intestinal damage in 1938, called attention to extensive extrinsic lesions observed in recent years. He attributed these changes to blood vessel damage resulting from irradiation of large fields with roentgen rays.

Although irradiation techniques have been much improved, and many protective devices are now in use, intestinal damage is still produced when vigorous attempts are made to cure advanced cases of cancer of the uterus. White[25] reported 7 such cases in 1940, and Wirth, Cantril and Buschke[26] observed 6 severe lesions in patients treated with supervoltage roentgen-ray equipment from 1935 to 1938. A very recent report by Cosbie,[5] published in 1941, covers a group of patients treated since 1936, with modern apparatus, and includes 11 cases of severe proctitis, with 12 cases of rectal ulceration with hemorrhage and stenosis. The protection of the intestinal tract requires much skill when heavy doses of roentgen rays are delivered directly into the pelvis with a vaginal cone, and Merritt, in reviewing this technique in 1941, stated that diarrhea with extreme debility was observed in certain individuals, while others developed a radiosclerosis of the sigmoid. Stone and Robinson[21] voice the opinion of many of the more competent radiologists when, in discussing the treatment of advanced carcinoma of the cervix, they state: "The consequences of excessive irradiation of the bladder and rectum must be disregarded because these structures or adjacent tissues are involved."

The mucous membranes of the bladder and ureters are very radiosensitive, but reports of serious injuries of these structures appear with relative infrequency in the literature. Schmitz[19] reported the obstruction of one ureter by a process which he designated as radiation fibrosis in 1920. A death from uremia, secondary to necrosis of the trigone and obstruction of both ureters, occurred in our own clinic in 1925, and a study of the tolerance of the ureters to radiation was started soon afterwards. In 1926[14] we were able to show that a dose of 75 miligram-hours administered by two 6.25 mg. monel steel radium needles placed on either side of the dog's ureter produced complete occlusion and hydronephrosis. However, a subsequent experiment[15] done in the same year showed that 2.5 T.E.D. applied directly to the ureter, with a heavily filtered capsule produced no damage. No information is available covering the maximum dose of heavily filtered radium which is safe for the ureters.

Ureteral stricture is a common complication in cancer of the cervix, and many radiologists believe that all such lesions in treated cases are produced by cancer. However, Everett[7] after studying the patients treated successfully with irradiation at the Howard A. Kelly Hospital in Baltimore, where high intensity radium applicators are used, concluded that approximately 50 per cent of these cases developed obstructive lesions involving the lower ureters with dilatation of the kidney pelves, but that only 15 per cent were sufficiently severe to

be of clinical importance. He also included in this report 63 cases of late irradiation ulceration of the bladder reported by Dean, Newell and Crossen, Smith and Colby, and described 6 cases observed in his own series.

Vesicovaginal and rectovaginal fistulae also often accompany cancer of the cervix when no irradiation is used, and the exact rôle of therapy in the causation of these unpleasant sequelae is difficult of estimation. Behney[1] reported an incidence of 26 per cent in treated cases and 31 per cent in untreated cases, and Smith,[20] after studying a series of 2,852 patients treated at the Memorial Hospital in New York, concluded that fistulae occurred at least twice as frequently in untreated as in irradiated cases. It is interesting to note that both of these reports cover work done prior to 1934 with techniques which were relatively conservative. Enough fistulae have been produced by the injudicious use of radium in the treatment of benign uterine lesions to make it apparent that such complications cannot always be attributed to the presence of cancer alone.

Vascular damage from irradiation has, in all probability, not received the attention that it deserves, since many of the necrotic lesions are undoubtedly preceded by an interference with blood supply. Emphasis was first placed on this complication in 1936 when Dalby, Jacox and Miller[6] described spontaneous fractures of the neck of the femur attributed to occlusion of the afferent vessels following the administration of heavy doses of roentgen rays to the pelvis. More recently Strauss and McGoldrick[22] have collected a series of 75 such cases, including 4 of their own. In most instances heavy doses of radium were used along with roentgen therapy, but a study of the treatment data indicates that this complication is likely to occur in patients receiving several prolonged series of roentgen treatments over the pelvis, particularly when lateral portals are used. Todd, in describing a condition which he calls an extrinsic lesion of the bowel, accompanied by extensive sclerosis, expresses the belief that blood vessel damage resulting from the application of heavy doses of roentgen rays to large portions of the pelvis is the causative factor.

Most cancers of the cervix contain pathogenic bacteria and a salpingitis is sometimes discovered when the patient presents herself for treatment. The manipulation of a bleeding vascular tumor of the cervix during the application of radium always carries with it the danger of dissemination of infection, and a conservative technique must be designed to minimize this danger.

TECHNIQUE

It is now evident that the radiotherapist treating cancer of the cervix is confronted with a problem which is far from simple. He must deliver a curative dose, estimated as not less than 7 T.E.D., to a structure bounded anteriorly by the bladder, posteriorly by the rectum and laterally by the ureters, all of which can be damaged by the therapeutic agent. When the disease extends outside the cervix, as it usually does, any attempt to efficiently irradiate a larger volume of tissue not only increases the hazards already mentioned, but endangers the vascular system supplying the bony structures and the pelvic viscera. The infected field in which all local manipulations must be carried out adds the danger of disseminated infection.

Since serious sequelae sometimes appear a year or more after treatment, the development of a safe technique is a slow procedure, based to a large extent on experience. In 1938 Corscaden, Kasabach and Lenz[4] made a careful study of irradiation injuries observed in their cases and published a technique which eliminated them. This was done by decreasing the intensity of irradiation and increasing the time. During the past ten years an attempt has been made in our clinic to eliminate the serious complications without lowering the total five year survival rate. Some of the technical changes may be lised as follows:

1. Use of multiple radium sources of moderate intensity for longer periods of time.
2. Frequent shifting of the positions of radium containers of the higher intensities.

3. Heavy filtration in all radium containers.
4. Distance applicators in the vagina used with large vaginal packs.
5. Removal of all presenting tumor tissues so that a smaller total radium dosage is effective.
6. Careful approximation of radium sources to malignant tissue.
7. Copious use of green soap in vaginal preparation for radium.
8. Frequent changing of vaginal packs.
9. No radon implants used and no radium needles placed near ureters.
10. Intensive roentgen therapy used only in more advanced cases.
11. Elimination of lateral portals in roentgen therapy.
12. Therapy given in one carefully planned series, and not repeated.
13. Long interval allowed to elapse between intensive roentgen therapy and radium therapy.
14. No intravaginal or perineal roentgen therapy administered.

During January, 1942, a survey was made of 149 consecutive unselected cases treated during the years 1936 to 1940 inclusive. Since untoward results almost always appear within two years, no case treated since 1940 was included. The techniques used were individualized as shown in the tables. Although roentgen therapy was usually given, the most effective part of the treatment was carried out with carefully placed radium applicators, prepared to irradiate all of the diseased tissue when possible. In the more diffuse lesions weak platinum radium needles, completely described in previous articles,[16] were used alone or in combination with platinum radium capsules having a wall thickness of 1.0 mm. Most of the radium treatments were given with capsules of various sizes containing from 6.25 to 50 mg. applied singly or in various combinations. The vaginal applications were made with London spools or specially prepared applicators, constructed so as to afford ample protection to the bladder and rectum. Needle implantations were made for a period of seven days. The average case treated with capsules received about eighty hours of irradiation, divided into three applications spaced a day apart. The total dose varied from 3,600 to 4,100 mg-hr. Capsules containing 50 mg. were left in the cervical canal for thirty hours, but the cervical and vaginal applicators contained multiple sources which were never left in one place for more than twenty-four hours. Cervical and vaginal applicators were never used on the same day.

The first radium application was always done under gas anesthesia. Before any manipulations were carried out the vagina and the tumor were washed repeatedly with copious amounts of green soap. This procedure is considered most important because serious post-irradiation infections were reduced to a minimum following its adoption. The entire field was next painted with tincture of iodine and the presenting portion of the tumor was destroyed by

TABLE I

SURVEY OF CANCER OF CERVIX MADE IN JANUARY, 1942

Year Treated	No. of Patients Treated	Known Dead	Untraced	Complications Possibly Due to Irradiation	Alive	
					Total Number	Symptom-free with No Evidence of Cancer
1936	32	4	13	2 fistulae	15—46.7%	14—43.7%
1937	27	7	11	1 fistula	9—33.3%	8—30%
1938	30	6	8	1 fistula	16—53.3%	14—46.6%
1939	32	8	6	0	18—56.2%	17—53.1%
1940	28	6	5	0	17—51.0%	12—42.8%
Total	149	31	43	4 fistulae	78—52.4%	65—43.2%

Table II

Tabulation of Cases

Case	Treatment Started	Primary Lesion	Pathology	Extension	Roentgen Rays r	Radium mg-hr.	Observed	Last Examination	Outcome
Patients treated in 1936									
1. A.D.	1- 9-36	Whole cervix; vaginal wall	Squam. II	Both ligaments	4 × 600	Capsules 3400	4 mo.	Cervix healed	Dead
2. R.E.D.	1-23-36	Face of cervix	Squam.	Both ligaments slight	4 × 520 2 × 2400	Capsules 4100	1 yr.	Cervix healed; abdominal mass	Untraced
3. A.B.	2- 4-36	Whole cervix	Squam. III	Lt. ligament slight		Needles 6048 Capsules 1000	5 yr. 10 mo.	No evidence of cancer	Alive
4. C.S.	2- 4-36	½" ulcer	Squam. II	None	4 × 600	Capsules 3600	5 yr. 10 mo.	No evidence of cancer	Alive
5. H.Mc.	2- 8-36	Cervix; upper vagina	Squam. II	Both ligaments	3 × 600 4 × 2000	Needles 4032 Capsules 2200	1 yr.	Deep pelvic involvement	Untraced
6. E.S.D.	2-10-36	Whole cervix	Squam. IV	Both ligaments slight		Capsules 4620	5 yr. 10 mo.	No evidence of cancer	Alive
7. M.Y.	3-14-36	Whole cervix	Squam. II	None		Needles 5645 Capsules 3000	1 yr.	Deep pelvic involvement	Untraced
8. A.T.	3-16-36	Whole cervix	Squam. II	Lt. ligament	4 × 600	Capsules 3600 Needles 3224	5 mo.	Deep pelvic involvement	Untraced
9. W.S.	3-16-36	Whole cervix	Squam. II	None	4 × 600	Capsules 3550	5 yr. 9 mo.	No evidence of cancer	Alive
10. W.T.W.	3-17-36	Cervical canal	Squam. II	?Both ligaments	4 × 600	Capsules 3600	5 yr. 9 mo.	? of local recurrence	Alive
11. F.E.	3-18-36	Whole cervix	Squam. III	None	4 × 600	Capsules 3900	1 yr.	Local recurrence	Dead
12. A.G.	4- 6-36	Whole cervical stump	Squam. II	Lt. ligament	4 × 1200	Needles 4838	5 yr. 8 mo.	No evidence of cancer	Alive
13. A.G.	4-22-36	Large cervical crater	Squam. I	Rt. ligament		Needles 4032	6 mo.	No healing	Untraced
14. J.P.R.	4-22-36	½" ulcer	Squam.	None	4 × 600	Capsules 3600	5 yr. 8 mo.	No evidence of cancer	Alive
15. R.H.	5- 4-36	Nodular cervix	Squam. II	Both ligaments	4 × 1200	Capsules 3600	2 yr. 9 mo.	Rectovag. fistula-recur.	Untraced
16. M.E.S.	7- 2-36	Post. radium recurrence	Squam.	Both ligaments	4 × 600	Capsules 2850	3 mo.	Deep pelvic extension	Untraced
17. B.H.	8- 1-36	Small nodular cervix	Squam. II	None		Needles 4550	5 yr. 4 mo.	No evidence of cancer	Alive
18. A.M.R.	8-21-36	Whole cervix; vaginal wall	Squam. II	None	4 × 600	Capsules 3100	5 yr. 4 mo.	No evidence of cancer	Alive
19. C.W.	9- 1-36	Whole cervix	Squam. II	None	3 × 560	Capsules 3600	5 yr. 3 mo.	No evidence of cancer	Alive
20. R.B.W.	9- 8-36	Cervix and upper vagina	Squam. II	Both ligaments	4 × 600 4 × 2000	Capsules 2900	6 mo.	Bladder involvement; hydronephrosis	Untraced
21. S.G.	9-14-36	Large cervical crater	Squam. II	Both ligaments	4 × 600	Capsules 2700	4 mo.	Deep pelvic extension	Untraced
22. B.B.R.	9-28-36	Whole cervix	Squam. III	Both ligaments—slight	4 × 600	Capsules 3500	2 mo.	Local improvement	Untraced
23. W.E.T.	10-19-36	Whole cervix; upper vagina	Squam. III	None	4 × 600	Capsules 3400	5 yr. 2 mo.	Vesicovag. fistula repaired; no cancer	Alive
24. M.C.	10-19-36	1" mass vaginal wall	Adenoca. I	Bladder		Needles 4836		Did not return	Untraced
25. J.M.B.	10-20-36	Whole cervix; vaginal wall	Squam. III	None	4 × 600	Capsules 3600	6 mo.	Cervix healed—abdom. mass	Untraced
26. Z.D.	10-29-36	Whole cervix; upper vagina	Squam. II	Both ligaments—slight	4 × 600 4 × 2000	Capsules 3700	10 mo.	Deep pelvic extension	Untraced
27. B.W.	11- 2-36	Whole cervix; vaginal wall	Squam. III	None	4 × 600	Capsules 3600	5 yr. 1 mo.	No evidence of cancer	Alive
28. J.D.L.	11- 2-36	½" mass	Squam. II	None	4 × 600	Capsules 3700	5 yr. 1 mo.	No evidence of cancer	Alive
29. C.S.B.	11-17-36	Whole cervix	Squam. II	Both ligaments	6 × 2000	Needles 5640 Capsules 1650	1 yr. 9 mo.	Deep pelvic extension	Dead
30. J.C.D.	11-19-36	½" mass cervical stump	Squam. III	None	4 × 600	Capsules 2300	5 yr. 1 mo.	No evidence of cancer	Alive
31. G.B.	11-30-36	Whole cervix	Squam. II	None	4 × 600	Capsules 4600	9 mo.	No evidence of cancer	Died of pneumonia
32. J.S.P.	11-30-36	1" mass	Squam. II	None	4 × 600	Capsules 3600	5 yr. 1 mo.	No evidence of cancer	Alive
Patients treated in 1937									
1. W.C.K.	1-25-37	Mass filling upper vagina	Squam. III	Both ligaments	4 × 600	Capsules 4000	2 mo.	No healing	Untraced
2. S.H.	2- 4-37	½ cervix; vaginal wall	Squam. IV	None	4 × 600	Capsules 3600	4 yr. 10 mo.	No evidence of cancer	Alive
3. R.C.	2- 6-37	1" mass	Squam. III	None	4 × 600	Capsules 3800	4 yr. 10 mo.	No evidence of cancer	Alive
4. L.B.	2-15-37	Whole cervix; vaginal wall	Squam. III	Both ligaments	4 × 600	Needles 6048	2 mo.	Local healing	Untraced
5. M.B.	2-15-37	Whole cervix; vaginal wall	Squam. III	Both ligaments	4 × 600	Capsules 3600	5 yr. 10 mo.	No evidence of cancer	Alive
6. M.B.	2-15-37	Whole cervix; vaginal wall	Squam. III	Both ligaments	4 × 600	Capsules 3600	5 yr. 10 mo.	No evidence of cancer	Alive
7. M.B.	2-15-37	Whole cervix; vaginal wall	Squam. III	Both ligaments	4 × 600	Capsules 3600	5 yr. 10 mo.	No evidence of cancer	Alive
8. M.B.	2-15-37	Whole cervix; vaginal wall	Squam. III	Both ligaments	4 × 600	Capsules 3600	5 yr. 10 mo.	No evidence of cancer	Alive
9. M.B.	2-15-37	Whole cervix; vaginal wall	Squam. III	Both ligaments	4 × 600	Capsules 3600	5 yr. 10 mo.	No evidence of cancer	Alive
10. M.B.	2-15-37	Whole cervix; vaginal wall	Squam. III	Both ligaments	4 × 600	Capsules 3600	5 yr. 10 mo.	No evidence of cancer	Alive
11. M.B.	2-15-37	Whole cervix; vaginal wall	Squam. III	Both ligaments	4 × 600	Capsules 3600	5 yr. 10 mo.	No evidence of cancer	Alive
12. M.B.	2-15-37	Whole cervix; vaginal wall	Squam. III	Both ligaments	4 × 600	Capsules 3600	5 yr. 10 mo.	No evidence of cancer	Alive
13. M.B.	2-15-37	Whole cervix; vaginal wall	Squam. III	Both ligaments	4 × 600	Capsules 3600	5 yr. 10 mo.	No evidence of cancer	Alive
14. M.B.	2-15-37	Whole cervix; vaginal wall	Squam. III	Both ligaments	4 × 600	Capsules 3600	5 yr. 10 mo.	No evidence of cancer	Alive
15. M.B.	2-15-37	Whole cervix; vaginal wall	Squam. III	Both ligaments	4 × 600	Capsules 3600	5 yr. 10 mo.	No evidence of cancer	Alive
16. M.B.	2-15-37	Whole cervix; vaginal wall	Squam. III	Both ligaments	4 × 600	Capsules 3600	5 yr. 10 mo.	No evidence of cancer	Alive
17. M.B.	2-15-37	Whole cervix; vaginal wall	Squam. III	Both ligaments	4 × 600	Capsules 3600	5 yr. 10 mo.	No evidence of cancer	Alive
18. M.B.	2-15-37	Whole cervix; vaginal wall	Squam. III	Both ligaments	4 × 600	Capsules 3600	5 yr. 10 mo.	No evidence of cancer	Alive
19. M.B.	2-15-37	Whole cervix; vaginal wall	Squam. III	Both ligaments	4 × 600	Capsules 3600	5 yr. 10 mo.	No evidence of cancer	Alive
20. M.B.	2-15-37	Whole cervix; vaginal wall	Squam. III	Both ligaments	4 × 600	Capsules 3600	5 yr. 10 mo.	No evidence of cancer	Alive
21. M.B.	2-15-37	Whole cervix; vaginal wall	Squam. III	Both ligaments	4 × 600	Capsules 3600	5 yr. 10 mo.	No evidence of cancer	Alive
22. M.B.	2-15-37	Whole cervix; vaginal wall	Squam. III	Both ligaments	4 × 600	Capsules 3600	5 yr. 10 mo.	No evidence of cancer	Alive
23. M.B.	2-15-37	Whole cervix; vaginal wall	Squam. III	Both ligaments	4 × 600	Capsules 3600	5 yr. 10 mo.	No evidence of cancer	Alive
24. M.B.	2-15-37	Whole cervix; vaginal wall	Squam. III	Both ligaments	4 × 600	Capsules 3600	5 yr. 10 mo.	No evidence of cancer	Alive
25. M.B.	2-15-37	Whole cervix; vaginal wall	Squam. III	Both ligaments	4 × 600	Capsules 3600	5 yr. 10 mo.	No evidence of cancer	Alive
26. M.B.	2-15-37	Whole cervix; vaginal wall	Squam. III	Both ligaments	4 × 600	Capsules 3600	5 yr. 10 mo.	No evidence of cancer	Alive
27. M.B.	2-15-37	Whole cervix; vaginal wall	Squam. III	Both ligaments	4 × 600	Capsules 3600	5 yr. 10 mo.	No evidence of cancer	Alive
28. M.B.	2-15-37	Whole cervix; vaginal wall	Squam. III	Both ligaments	4 × 600	Capsules 3600	5 yr. 10 mo.	No evidence of cancer	Alive
29. M.B.	2-15-37	Whole cervix; vaginal wall	Squam. III	Both ligaments	4 × 600	Capsules 3600	5 yr. 10 mo.	No evidence of cancer	Alive
30. M.B.	2-15-37	Whole cervix; vaginal wall	Squam. III	Both ligaments	4 × 600	Capsules 3600	5 yr. 10 mo.	No evidence of cancer	Alive
31. M.B.	2-15-37	Whole cervix; vaginal wall	Squam. III	Both ligaments	4 × 600	Capsules 3600	5 yr. 10 mo.	No evidence of cancer	Alive
32. M.B.	2-15-37	Whole cervix; vaginal wall	Squam. III	Both ligaments	4 × 600	Capsules 3600	5 yr. 10 mo.	No evidence of cancer	Alive

1. W.C.K.	1-25-37	Mass filling upper vagina	Squam. III	Both ligaments	4 X 600	Capsules 4000	2 mo.	No healing	Untraced
2. S.H.	2- 4-37	½ cervix; vaginal wall	Squam. IV	None	4 X 600	Capsules 3600	4 yr. 10 mo.	No evidence of cancer	Alive
3. R.C.	2- 6-37	1" mass	Squam. III	None	4 X 600	Capsules 3800	4 yr. 10 mo.	No evidence of cancer	Alive
4. T.J.F.	2-17-37	Whole cervical stump	Squam. III	Both ligaments	4 X1000	Needles 6048	3 mo.	Local healing	Untraced
5. H.H.W.	3- 4-37	Whole cervix	Squam. IV	None	4 X 600	Capsules 3600	4 yr. 9 mo.	Cervix healed; ligaments tense	Alive
6. H.O.R.	3-19-37	Small nodular cervix	Squam. II	Both ligaments	4 X1200	Capsules 3600	4 yr. 9 mo.	Cervix healed; ligaments tense	Alive
7. E.S.B.	3-20-37	Cervix and all of vagina	Squam. IV	Both ligaments	4 X1600	Capsules 2200	2 mo.	Local improvement	Untraced
8. T.O.M.	3-22-37	Whole cervix	Adenoca. II	Both ligaments	4 X2000	Capsules 2400	4 yr. 9 mo.	Cervix healed—ligament involv.?	Alive
9. L.R.	3-23-37	½" mass	Squam. III	None	4 X 600	Capsules 3600	6 mo.	No evidence of cancer	Dead—unknown cause
10. J.W.S.	4- 1-37	½" mass	Squam. III	None	4 X 600	Capsules 3750	4 yr. 8 mo.	No evidence of cancer	Alive
11. A.M.S.	4- 5-37	Cervical canal	Adenoca. III	None	4 X 600	Capsules 3450	4 yr. 8 mo.	No evidence of cancer	Alive
12. G.H.H.	4- 6-37	Whole cervix	Squam. III	None	4 X 600	Capsules 3500	4 yr. 8 mo.	No evidence of cancer	Alive
13. A.S.	4-13-37	Cervical canal	Squam. III	None	4 X 600	Capsules 3700	4 yr. 8 mo.	No evidence of cancer	Alive
14. L.T.	4-22-37	Small cervical crater	Squam.	Lt. ligament	4 X1800	Capsules 1500		Did not return	Dead
15. G.S.	5- 3-37	2" mass ant. lip	Squam. III	Pulmonary and abdominal	4 X 600	Capsules 3600	6 mo.	Local healing	Untraced
16. E.D.	5-22-37	Whole cervix	Squam. III	Both ligaments	4 X 600	Capsules 3600		Did not return	Untraced
17. L.S.	7-12-37	Cervical canal	Adenoca. III	Both ligaments	4 X 600	Capsules 3300	2 mo.	Local healing	Untraced
18. D.E.	7-24-37	Whole cervix	Squam. IV	Lt. ligament	4 X 600	Capsules 4800	3 mo.	Vesicouterine fistula; local healing	Died 3 yr. later
19. T.L.H.	7-29-37	Whole cervix	Squam. III	Both ligaments		Needles 5614	4 mo.	Local healing	Dead
20. M.J.T.	8-18-37	½" crater	Squam. III	None	4 X 600	Capsules 4200	8 mo.	Deep pelvic extension	Dead
21. S.V.Mc.	9-19-37	Nodular cervix	Squam. III	Both ligaments	4 X2000 4 X1500	Capsules 4200	8 mo.	Deep pelvic extension	Untraced
22. L.M.	9-22-37	Large crater	Squam. III	Both ligaments; uremia	4 X 800	Capsules 3900	8 days	No change	Dead
23. A.P.B.	9-27-37	Whole cervix	Squam. III	Both ligaments	4 X 600 4 X2500	Capsules 3600	6 mo.	Local healing Ligament unchanged	Untraced
24. J.M.J.	10- 7-37	Whole cervix	Squam. IV	Lt. ligament	4 X 600 4 X3000	Capsules 3600 Needles 3952	7 mo.	Local healing Ligament unchanged	Untraced
25. J.S.	10-15-37	Whole cervix	Squam. III	Both ligaments	4 X 600	Capsules 3900	1 yr. 1 mo.	Local healing; deep extension	Untraced
26. O.M.J.	11- 8-37	Whole cervix; vaginal wall	Squam. I	None	4 X 600	Capsules 3600	3 mo.	No evidence of cancer	Untraced
27. E.W.	11-22-37	Whole cervix; vaginal wall	Squam. III	None	4 X 600	Capsules 3800		Did not return	Dead

PATIENTS TREATED IN 1938

1. G.H.	1- 4-38	Whole cervix	Squam. III	None	4 X 600	Capsules 4100	3 yr. 11 mo.	No evidence of cancer	Alive
2. H.C.H.	1-17-38	2" pedunculated mass	No report	None	4 X 600	Capsules 4100	11 mo.	No evidence of cancer	Dead—kidney stone
3. J.T.B.	1-18-38	½" crater	Squam. III	None	4 X 600	Capsules 3900 Capsules 1800	18 mo.	Deep extension	Untraced
4. W.S.C.	2- 3-38	Whole cervix	Squam. II	None	4 X 600	Capsules 3600	3 yr. 10 mo.	Cervix healed; lt. ligament tense	Alive
5. H.H.J.	2- 4-38	Whole cervix	Squam. I	Ligaments doughy	4 X 600	Capsules 4500	3 yr. 10 mo.	No evidence of cancer	Alive
6. E.H.	2- 8-38	Indurated cervical stump	Squam. III	None	4 X 600 12 X 210	Capsules 3600 Needles 4628	3 yr.	Rectovag. fistula Deep. Extension	Dead
7. M.L.	2-16-38	2" mass cervical stump	Adenoca. I	Ligaments tense	4 X 250	Needles 4628	3 yr. 10 mo.	No evidence of cancer	Alive
8. H.C.B.	2-21-38	Whole cervical stump	No report	Both ligaments	4 X2100	Needles 5624	2 yr. 1 mo.	Cervix healed; deep extension	Untraced
9. A.D.H.	2-22-38	Ant. lip	Squam.	None	4 X 600	Capsules 3800	3 yr. 10 mo.	Cervix healed; ligaments tense	Alive
10. A.J.Y.	3- 4-38	Whole cervix	Squam. III	None	4 X 400	Capsules 4100	1 yr.	Deep pelvic extension	Untraced
11. G.M.H.	3- 4-38	Whole cervix; vaginal walls	Squam. III	Both ligaments	4 X 400	Capsules 3700	5 mo.	Vaginal recurrence	Untraced
12. J.I.B.	3- 7-38	Whole cervix	Squam. III	Both ligaments	4 X2200	Treat. Incomplete		Did not return	Untraced
13. D.N.B.	3-11-38	Whole cervix	Adenoca. II	Lt. ligament	4 X 400	Capsules 3700	5 mo.	No evidence of cancer	Untraced
14. J.H.B.	3-31-38	Whole cervix	Squam. III	Both ligaments	4 X 250	Capsules 3600	1 yr. 4 mo.	Cervix healed; ligaments tense	Dead
15. H.S.S.	4- 4-38	Massive tumor	Squam. IV	Both ligaments	4 X3000	Capsules 1200	1 yr.	Marked improvement	Dead
16. J.W.P.	4-11-38	Whole cervix	Squam. II	None	4 X 250 4 X2200	Capsules 4000	3 yr. 8 mo.	No evidence of cancer	Alive

TABLE II—*Continued*

Case	Treatment Started	Primary Lesion	Pathology	Extension	Roentgen Rays r	Radium mg-hr.	Observed	Last Examination	Outcome
				PATIENTS TREATED IN 1938—(*Continued*)					
17. S.P.G.	4-11-38	Whole cervix	Squam. IV	None	4 × 250	Capsules 4000	3 yr. 8 mo.	No evidence of cancer	Alive
18. J.H.B.	4-20-38	Cervical canal	Squam. III	None	4 × 250	Capsules 3800	3 yr. 8 mo.	No evidence of cancer	Alive
19. E.M.C.	4-25-38	High cervical canal	Squam. III	Both ligaments	4 × 250 4 × 2000	Capsules 4100	3 yr. 8 mo.	Deep extension Ureteral stricture	Dead
20. L.J.	4-28-38	Post. lip; vaginal walls	Squam. III	None	4 × 250 4 × 2200	Capsules 3600	3 yr. 7 mo.	No evidence of cancer	Alive
21. J.B.H.	5- 7-38	¾″ mass post. lip	Squam. I	None	4 × 600	Capsules 3600	3 yr. 7 mo.	No evidence of cancer	Alive
22. R.H.J.	5-18-38	2″ mass ant. lip	Squam. III	None	4 × 600	Capsules 4350	3 yr. 7 mo.	No evidence of cancer	Alive
23. T.D.C.	6- 6-38	Cervical canal	Squam. I	None	4 × 600	Capsules 3600	3 yr. 6 mo.	No evidence of cancer	Alive
24. R.P.	6-16-38	Ant. lip	Squam.	None	4 × 600	Capsules 3700		Did not return	Untraced
25. N.F.	6-20-38	1½″ mass; vaginal wall	Squam. III	Ligaments doughy	4 × 250 4 × 2250	Capsules 3800	3 yr. 6 mo.	No evidence of cancer	Alive
26. I.A.	6-24-38	Whole cervix	Squam. I	Both ligaments	4 × 600 4 × 600	Capsules 4200 Needles 4433	1 yr.	Local recurrence	Untraced
27. M.D.W.	7- 4-38	1½″ mass post. lip	Squam. III	Lt. ligament	4 × 600	Capsules 2800	2 mo.	Cervix healed; deep extension	Died 3 yr. later
28. J.R.C.	9-20-38	Whole cervix	No report	Lt. ligament	4 × 250	Capsules 4000	3 yr. 3 mo.	No evidence of cancer	Alive
29. J.F.L.	10-17-38	Whole cervix	Squam. I	Lt. Ligament	4 × 600	Capsules 4100 Capsules 2400	3 yr. 2 mo.	Cervix healed; ligament tense	Alive
30. D.E.Mc.	11-25-38	½ cervix	Squam. III	None	4 × 600	Capsules 3800	3 yr. 1 mo.	No evidence of cancer	Alive
				PATIENTS TREATED IN 1939					
1. W.H.M.	1-16-39	Nodular cervix	Squam. III	Lt. ligament	4 × 600	Capsules 3000 Capsules 2000	6 mo.	Deep pelvic extension	Dead
2. R.L.J.	1-16-39	1″ mass	Squam. III	None	4 × 600	Capsules 3600	2 yr. 11 mo.	No evidence of cancer	Alive
3. B.K.	1-29-39	Whole cervix; vaginal wall	Squam. III	None	4 × 600	Capsules 4200	4 mo.	No evidence of cancer	Dead
4. B.Mc.	1-31-39	Whole cervix; vaginal wall	Squam. II	None	4 × 600	Capsules 3800	2 yr. 11 mo.	No evidence of cancer	Alive
5. F.W.	2-14-39	Cervical canal	Squam. III	None	2 × 250	Capsules 5100	2 yr. 10 mo.	No evidence of cancer	Alive
6. W.M.S.	2-15-39	3″ mass	Squam. III	?Ligaments slight	4 × 600	Capsules 4400	2 yr. 10 mo.	No recent examination	Alive
7. E.W.	3-17-39	Large crater	Squam. IV	Lt. ligament Hydronephrosis		Needles 5239	6 wks.	No improvement	Untraced
8. M.F.M.	4- 3-39	Cervical canal	Adenoca. I	None	4 × 600	Capsules 4200	2 yr. 8 mo.	No evidence of cancer	Alive
9. V.F.Mc.	5- 5-39	Whole cervix	Squam. II	Lt. ligament	2 × 2800	Needles 5642 Capsules 1000	9 mo.	Deep pelvic extension	Untraced
10. C.A.C.	5-27-39	Cervical canal	Adenoca. I	None	4 × 600	Capsules 3600	2 yr. 7 mo.	No evidence of cancer	Alive
11. E.W.S.	5-29-39	Whole cervix; vaginal wall	Adenoca. I	Lt. ligament	4 × 600	Capsules 4200	2 yr. 7 mo.	No evidence of cancer	Alive
12. H.H.	5-29-39	¾″ mass cerival stump	Squam. IV	?Ligaments slight		Capsules 600 Needles 4032	2 yr. 7 mo.	No evidence of cancer	Alive
13. M.O.	6- 1-39	Nodular cervix; vaginal wall	Squam. III	Lt. ligament	4 × 600 4 × 3120	Capsules 3900	2 yr.	Deep pelvic extension	Dead
14. B.L.	6-10-39	Whole cervix	Squam. IV	Lt. ligament	4 × 600	Capsules 4200	2 yr. 6 mo.	No evidence of cancer	Alive
15. A.D.	6-27-39	Whole cervix	Adenoca. I	None	4 × 600	Capsules 3900	2 yr. 6 mo.	No evidence of cancer	Alive
16. A.D.E.	7-22-39	Whole uterus	Squam. II	Lt. ligament	2 × 600	Needles 6448	2 mo.	Marked improvement	Dead
17. Z.M.N.	7-24-39	Large crater	Squam. III	Both ligaments	4 × 600 4 × 2550	Capsules 4000	4 mo.	Much improvement	Dead
18. F.D.	7-25-39	1½″ mass post. lip	Squam. III	None	4 × 600	Capsules 3900	2 yr. 5 mo.	No evidence of cancer	Alive

18. F.D.	7-25-39	1¾" mass post. lip	Squam. III	None	4 × 2550 4 × 600	Capsules 3900	2 yr. 5 mo.	No evidence of cancer	Alive
19. C.S.	7-27-39	Crater in nodular cervix	Squam. IV	None	4 × 600	Capsules 3900	2 yr. 5 mo.	No evidence of cancer	Alive
20. E.V.K.	8- 8-39	Whole cervix	Squam. III	Both ligaments	4 × 600 2 × 900	Capsules 4200 Needles 3627	7 mo.	Deep pelvic extension	Dead
21. J.C.	8-19-39	Whole cervix	Squam. III	Lt. ligament	2 × 2400	Needles 2418 Capsules 2700	4 mo.	Local healing	Untraced
22. V.R.	9- 1-39	Large crater	Squam. II	Lt. ligament	10 × 210	Capsules 4300	2 yr. 3 mo.	No evidence of cancer	Alive
23. B.T.	9-14-39	Whole cervix	No report	Both ligaments		Needles 5239	9 mo.	Deep pelvic extension	Dead
24. C.N.	9-29-39	Large nodular cervix	Squam. II	Ligaments tense	4 × 600	Capsules 4500	2 yr. 3 mo.	Cervix healed; deep recurrence	Alive
25. J.M.O.	9-30-39	Nodular cervix	Squam. IV	None	4 × 600 6 × 210	Capsules 4200 Capsules 2250	3 mo.	Deep pelvic extension	Dead
26. J.A.D.	10-11-39	Whole cervical stump	Squam. IV	Both ligaments	4 × 600	Needles 5642		Did not return	Untraced
27. L.H.	11-11-39	Whole cervix	Squam. III	Lt. ligament	2 × 1470 6 × 1470	Needles 6048	1 yr. 2 mo.	Deep pelvic tumor	Untraced
28. H.M.H.	11-11-39	Cervical canal	Squam. III	None	4 × 600	Capsules 3600	1 yr.	No evidence of cancer	Untraced
29. D.B.	11-15-39	Polypoid mass	Squam. III	None	4 × 600	Capsules 3600	2 yr. 1 mo.	No evidence of cancer	Alive
30. J.Y.E.	11-18-39	Whole cervical stump	Squam. II	None	2 × 1260	Needles 3627	2 yr. 1 mo.	No evidence of cancer	Alive
31. J.S.B.	11-26-39	Whole cervix	Squam. III	Lt. ligament	2 × 1260	Needles 5239	2 yr. 1 mo.	Deep extension; hydronephrosis	Alive
32. C.D.J.	12- 1-39	¼" mass	Squam. III	None	4 × 600	Capsules 5100	2 yr.	No evidence of cancer	Alive

PATIENTS TREATED IN 1940

1. J.A.P.	1- 1-40	Whole cervix	Squam.	None	4 × 600	Capsules 3700	2 yr.	No evidence of cancer	Alive
2. M.A.B.	1- 5-40	Nodular cervix	Squam. II	None	4 × 600	Prescription lost		Did not return	Untraced
3. E.R.	1-26-40	Whole cervix; vaginal wall	Squam. II	?Slight ligament involvement	4 × 600 4 × 2100	Capsules 4000	2 yr.	Local healing; hydronephrosis	Alive
4. W.G.	1-31-40	Small ulcer	Squam. III	None	4 × 600	Capsules 3700	1 yr. 11 mo.	No evidence of cancer	Alive
5. P.R.J.	2-16-40	Post. lip; vaginal wall	Squam. III	None	4 × 600	Capsules 3900	1 yr. 10 mo.	No evidence of cancer	Alive
6. E.D.	2-23-40	Large crater	Squam.	Both ligaments	4 × 600	Capsules 2100	6 mo.	Deep pelvic extension	Dead
7. M.H.G.	2-24-40	Nodular cervix	Squam. III	None	4 × 600	Capsules 4250		Did not return	Untraced
8. A.Mc.	2-26-40	Whole cervix	Squam. IV	None	4 × 600	Capsules 3900	1 yr. 10 mo.	No evidence of cancer	Alive
9. W.H.K.	2-29-40	Cervical canal	Squam. III	Lt. ligament	4 × 600	Capsules 3700	1 yr. 10 mo.	Cervix healed; lt. ligament involv.?	Alive
10. V.E.Mc.	3- 9-40	½" cervix	Squam. III	?Lt. ligament	2 × 1200 4 × 2250	Capsules 3800	1 yr. 9 mo.	No evidence of cancer	Alive
11. J.C.C.	3-23-40	Whole cervix	Squam. II	None	4 × 600	Capsules 3600		Did not return	Untraced
12. R.L.A.	4-18-40	Whole cervix; vaginal wall	Squam. III	Lt. ligament	4 × 600	Capsules 3450	1 yr. 8 mo.	Cervix healed; ligament tense	Alive
13. W.P.H.	5- 2-40	Nodular cervix	Squam. III	Lt. ligament	4 × 600	Capsules 4100	6 mo.	No evidence of cancer	Alive
14. B.M.	5-24-40	Cervix; vaginal and bladder	Adenoca. II	Lt. ligament	4 × 600	Capsules 4000	11 mo.	Cervix healed; mass in pelvis	Dead
15. S.F.H.	5-27-40	Whole cervix	Squam. II	Both ligaments	4 × 600 4 × 3000	Capsules 3900	7 mo.	Frozen pelvis	Dead
16. F.P.	6-13-40	Large crater	No report	Both ligaments	4 × 600	Capsules 3800		Did not return	Dead
17. A.B.H.	6-18-40	Cervical canal	Squam. IV	None	4 × 600	Capsules 4300	1 yr. 6 mo.	No evidence of cancer	Alive
18. R.J.G.	7-10-40	Whole cervix	Squam. III	Both ligaments	4 × 600	Capsules 4500	1 yr. 5 mo.	Bladder and ligament involv.	Alive
19. S.C.S.	7-25-40	Cervical canal	Adenoca. II	None		Capsules 3650 Needles 1612	1 yr. 5 mo.	No evidence of cancer	Alive
20. O.W.D.	7-27-40	Cervical canal	Squam. I	None	4 × 600	Capsules 3800	1 yr. 5 mo.	No evidence of cancer	Alive
21. J.C.Mc.	9-13-40	Malignant polyp	Squam.	None	4 × 1250	Capsules 3200	1 yr. 3 mo.	No evidence of cancer	Alive
22. R.D.	9-16-40	Ulcer external os	Squam. III	None	4 × 600	Capsules 3900	1 yr. 3 mo.	No evidence of cancer	Alive
23. C.A.P.	10-17-40	Cervical and vaginal walls	Squam. III	Both ligaments	4 × 3380	Capsules 1500	6 mo.	Local improvement	Dead
24. A.L.	10-18-40	Nodular stump	Squam. IV	Lt. ligament	2 × 1200	Needles 4433	2 mo.	Deep pelvic extension	Untraced
25. E.A.A.	10-19-40	Nodular cervix with crater	Squam. III	Both ligaments	4 × 600	Needles 5642	1 yr. 2 mo.	Cervix healed; deep extension	Alive
26. J.A.M.	10-22-40	Large mass in stump	Squam. III	None	2 × 1200	Needles 2010	1 yr. 2 mo.	No evidence of cancer	Alive
27. J.H.E.	11- 6-40	Whole cervix; vaginal wall	Squam. IV	Both ligaments	2 × 1200	Capsules 1200 Needles 6048	6 wk.	Frozen pelvis	Untraced
28. D.L.	11-14-40	Whole cervix; vaginal wall	Squam. III	Lt. ligament	4 × 3000			Did not return	Dead

electrocoagulation and removed with biting forceps. Although this procedure is condemned by many, it is considered an essential part of our technique because it enables the operator to place radium applicators accurately in intimate contact with the base of the tumor in a dry field, from which all confusing hemorrhage has been eliminated. It also makes it possible for him to obtain several biopsies of ample size from various portions of the neoplasm. A moderate temperature elevation usually follows the coagulation for a day or two. In the rare case in which a troublesome infection persists, sulphonamide therapy has been found quite effective.

Roentgen therapy was considered to be of secondary importance in the early and border line cases, but single doses of 600 r were given to each of four 15 cm. portals, using 200 kv. equipment, while the patient was hospitalized for radium therapy. Two portals were laid out over the front of the pelvis and two over the back. In most instances the radium applications and the roentgen treatments were given on alternate days. This plan was economical in that it enabled the patient to receive all of her therapy within a period of a week.

The cases which did not respond well to this procedure were rarely improved by the subsequent administration of more intensive roentgen therapy. Tod[24] made a similar observation and states that she obtained a higher percentage of cures in clinical Stages I and II when no roentgen therapy was added to her radium technique. The use of intensive preliminary roentgen therapy in these cases not only increases the incidence of irradiation sequelae, but produces so much contraction of the upper vaginal vault that London spools or other types of applicators designed to bring radium near the broad ligaments cannot be properly placed.

When the disease was well advanced, and particularly when there was much infection present, roentgen therapy was given first. In these cases palliation was the primary objective, and measures designed to relieve symptoms seemed more important than a vain attempt at a cure, followed by prolonged irradiation sequelae. In most instances four portals were used, as in the more favorable cases. Lateral portals were not used, because, in my opinion, they increase the danger of spontaneous hip fractures and add little to the efficiency of the treatment. Doses of 200 r were given to each of two portals daily, with 200 kv. equipment, until total amounts of 1,200 to 2,400 r had been administered to each area. When the smaller doses were given, the roentgen series was followed immediately by the radium therapy previously described, but radium applications were delayed for a period of three or four weeks when the more intensive external irradiation was utilized. Intravaginal roentgen therapy which of necessity increases the dosage reaching the anterior rectal wall was never used. A study of the histories of patients developing irradiation fractures of the hip indicates that most of them received repeated series of roentgen treatments given at intervals of six to eight weeks. For this reason it was assumed that the maximum palliation was produced when the above plan of treatment was completed, and further irradiation was rarely attempted. In those cases in which it was carried out, it seemed to be of little value. Certainly it should be delayed for a period of six to eight months, if it is to be given at all.

RESULTS

Although the technique described above is somewhat unorthodox, it should be judged by the results summarized in Table 1. Heyman[9] reports that the average five year survival rate in a group of 10,970 cases of carcinoma of the cervix, treated in the best irradiation clinics in the world, is 26 per cent. Although the group of cases reported in this paper is not large, and only a relatively small number have been followed for more than five years, the figures indicate that the five year survival rate will be as good as that averaged by other

clinics. Of more importance is the fact that the only complications which might be attributed to the effects of irradiation are four fistulae. Although 43 of the patients could not be traced during the entire period of observation, most of them were observed long enough to rule out the occurrence of irradiation sequelae. None of them developed rectal ulceration, bladder ulceration intestinal obstruction, serious infections or fractured hips. A fair number died with strictures of the ureters, but the incidence was no higher than that observed in untreated cases.

SUMMARY

An irradiation technique is described which produced end-results equal to those reported by other clinics, with no serious irradiation sequelae, except four fistulae. All techniques should be judged on the basis of irradiation complications, as well as five year survival rate.*

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* For discussion see page 515.

AN INSTRUMENT FOR INSERTING MULTIPLE CAPSULES OF RADIUM WITHIN THE UTERUS IN THE TREATMENT OF CORPUS CANCER*

By JAMES F. NOLAN, M.D., *and* A. N. ARNESON, M.D.
ST. LOUIS, MISSOURI

IT IS the opinion of several authors that the best clinical results obtained in the treatment of carcinoma of the body of the uterus have followed the combined use of both irradiation and surgery. One need only consult collected statistics that have been published to justify the value of irradiation.[1,13] It can be said, however, that removal of the uterus, whenever practical, remains the fundamental procedure. The addition of roentgen rays and radium in the treatment of operable cases compromises in no way the value of hysterectomy.

There is evidence that preoperative irradiation is more effective than treatment given after hysterectomy. One factor contributing to the relative superiority for preoperative irradiation must be the greater tissue dose that can be obtained by means of radium applied within the uterus before its removal. Corpus cancer, however, presents technical problems that often make difficult a satisfactory application of radium.

There is general agreement that an intrauterine tandem is ineffective in most instances. In spite of the fact that the active length of the applicator may extend from the top of the fundus to the external os, a bulky lesion may so distort the cavity that several centimeters of tissue intervene between some tumor cells and the radium sources. In cavities of normal size the tandem may be along the center of the uterus or fall toward one side. If there is a small lesion in one cornu there may be considerable distance between the tumor and nearest radium source. These factors are bound to produce marked irregularities in radiation effect. Gross specimens obtained after tandem treatment usually reveal focal areas of tumor destruction with other regions of unaffected cancer.[2] Due to the small number of sources employed, the contributions from each must be relatively great: For that reason radiation necrosis is not uncommon.

A logical method for increasing the effectiveness of radium treatment is the use of a greater number of sources placed irregularly throughout the uterine cavity. Several years ago, however, Sampson[15] demonstrated many of the difficulties encountered in the attempt to use multiple capsules. Others have feared injury to the uterus, chiefly by perforation of the wall. At the same time several authors including Heyman,[9] Schmitz and Schmitz,[16] Martin,[12] Brown,[4] Friedman,[7] Strauss,[17] Pfahler,[14] Crossen,[5] Kaplan,[11] and others, have devised special techniques of treatment. Most of these methods include the use of several sources of small size containing relatively small amounts of radium. Heyman's technique presents definite advantages. The small, weak, intra-uterine tubes are so constructed that an appreciable distance is obtained between the emanating source and outer wall of the applicator. These are packed singly into the uterine cavity until all available space has been filled.

In 1938 at both the Barnes Hospital and the Barnard Free Skin and Cancer Hospital we began the use of a method requiring a minimum of special apparatus.[2] The attempt was made to approximate the technique devised by Heyman. Radium sources of different size and strength were placed

* From the Department of Obstetrics and Gynecology, and the Edward Mallinckrodt Institute of Radiology, Washington University School of Medicine; and the Barnard Free Skin and Cancer Hospital, St. Louis, Mo. Presented at the Twenty-Seventh Annual Meeting, American Radium Society, Atlantic City, N. J., June 8–9, 1942.

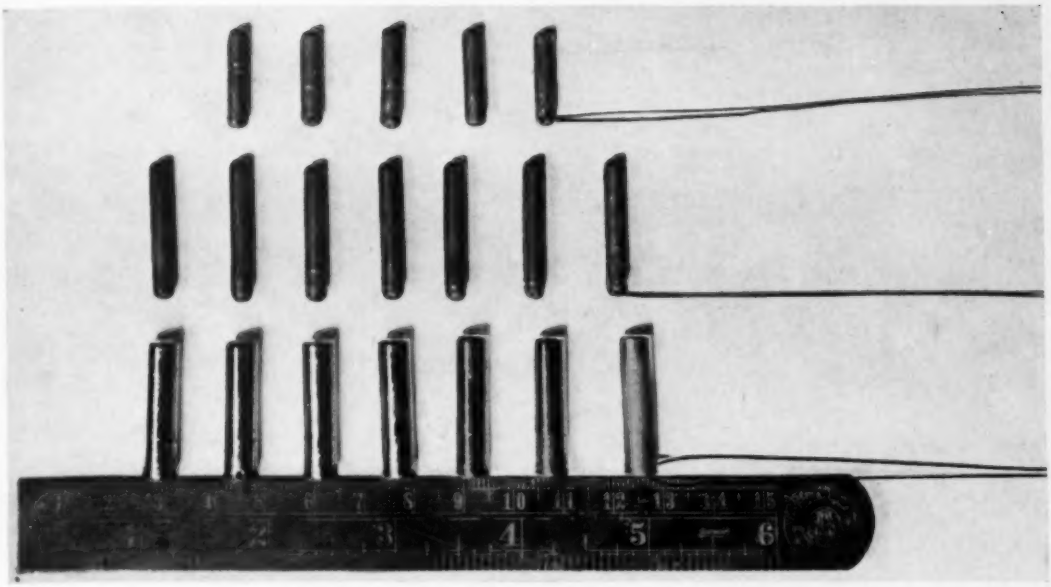

Fig. 1. Brass capsules used for intra-uterine treatment. The longer tubes are for one or more sources of 12.5 mg. radium strength. Those of greater diameter are used in the cervical canal. The shorter capsules contain 6.0 mg. radium in removable platinum cells.

within the uterus by means of uterine dressing forceps. Small strips of gauze were used in the attempt to keep the radium tubes in place, and also to obtain some distance around the stronger sources. Each application was checked by means of a roentgenogram. The method has not proved entirely satisfactory. In many instances it was difficult to get the tubes in place, and not infrequently rather marked irregularities in radiation effect were noted in specimens obtained at hysterectomy. The incidence of severe necrosis was, however, decidedly less than for tandems.

More recently the attempt has been made to improve the method. The points and eyelets of several monel metal needles were ground away to obtain sources with active lengths corresponding more closely to the over-all length of the tube. The shortened needles contain approximately 12.5 mg. radium each, and are about twice the length of removable platinum cells. Brass tubing was used to make sheaths of equal external diameters, but of different lengths. The longer brass sheaths will contain one of the 12.5 mg. sources, and the shorter ones hold 6.0 mg. in removable platinum cells. By that means several sources are obtained that contain approximately the same radium strength per centimeter length.

In some instances it may be advisable to employ stronger sources, or sheaths of greater external diameter. If the cervix is involved, for instance, it is more practical to use stronger tubes in that region because there are no others in parallel to contribute radiation. There should always be a sheath of greater diameter in the cervical canal to maintain dilatation adequate for removal of those of lesser diameter deeper in the uterus. For the above reasons several sheaths were made with external diameters about twice that of those first described and with internal diameters adequate for two of the 12.5 mg. tubes (total strength 25 mg. radium). A photograph of the sheaths of three different sizes is shown in Figure 1. The total filter for each, including the metal wall of the different radioactive tubes, is equivalent to 2.0 mm. brass.

It became necessary to devise an instrument for introducing radium into the

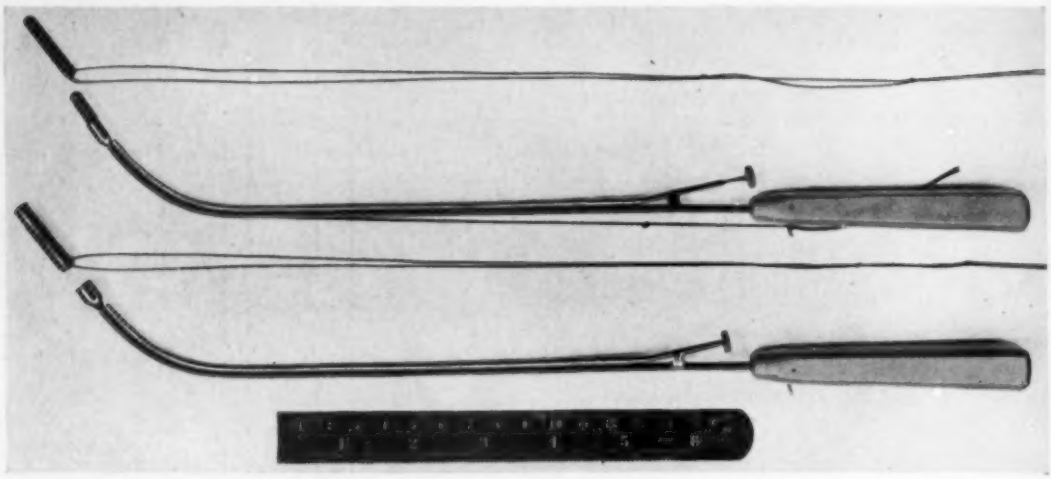

Fig. 2. Instruments used for inserting tubes of radium into the uterus.

uterus. A cup-shaped adapter was attached to a rod, or shank, curved to accommodate the angle of the uterus. A slit in the side of the cup provides an opening through which the ligature from the radium source can be fitted into a groove along the convex surface of the shank, and fixed to a small peg on the handle of the instrument. Along the concave surface of the shank is a small tube through which a wire ejector projects into the cup-shaped adapter. The ejector must be partially withdrawn for loading the instrument. After the radium is passed to the desired position within the uterus, the ligature is detached from the peg on the handle, and the ejector pressed in to discharge the source. Due to the fact that capsules of two different diameters are employed it is necessary to have introducers with adapters for each size. For convenience there should be more than one instrument of each size. A photograph of the introducers is shown in Figure 2. It should be noted that the use of multiple sources of radium within the uterus is not a new method of treatment. The technique presented here is essentially a modification of the method described by Heyman.[9]

From 1938 to 1941, inclusive, a total of 69 patients with cancer of the corpus uteri were treated with radium at the Barnard Free Skin and Cancer Hospital, and on the teaching service at the Barnes Hospital. There is no justification for attempting an analysis of clinical results, but the number of patients is believed adequate for a preliminary report upon the methods of treatment. During this period a transition was made from the use of intra-uterine tandems to multiple sources. Of the total number, tandems were employed in 24 patients, and multiple sources in 45. Among those in whom multiple tubes of radium were used, the earlier gauze method was employed in 36 individuals and the newer introducer in nine. It was during this period also that a transition was made to preoperative radium in all patients treated by hysterectomy. During the first half of the four year period a good many operable patients were treated by surgery alone, or in conjunction with roentgen irradiation. These are not here included, and their loss to radium treatment accounts for the relatively low hysterectomy rate to be shown later.

In Table 1 is shown the number of patients treated with radium applied by the different methods. With the exception of those in whom tandems were employed they have been grouped according to the depth of the uterine cavity. This is done to show variation in the average number of radium sources used, and in average total doses employed. It can be seen, that, for

multiple capsules, the number of sources placed in the uterus increases with depth of the cavity. For uteri of a given size the average number of sources is greatest among patients treated with the introducer devised recently. There is shown also an increase in average total dose with uterine cavities of greater depth. Among those measuring from 4 to 5 inches treated with the introducer, however, this increase is not apparent. That is due to the fact that only 2 patients fall into the group in question. One of those had been irradiated elsewhere, and only a small additional dose of radium was given prior to hysterectomy. The most significant finding in the table is the average dose per source. For tandems the amount contributed by each tube is enormous. Necrosis is to be expected. There is a marked decrease in dose per source among the first multiple-capsule treatments in which gauze was used. As a result the amount of necrosis was materially lessened, despite the fact that the minimum tumor dose was increased materially. There is evidence that the average dose per source will become even less among patients treated with the newer method.

TABLE I

TOTAL NUMBER OF PATIENTS TREATED WITH RADIUM FOR CORPUS CANCER FROM 1938 TO 1941, INCLUSIVE

Number of Cases	Depth of Uterus inches	Number of Sources	Total Dose mg-hr.	Dose per Source mg-hr.
		Intra-uterine Tandem		
24		2–3	4000	1800
		Multiple Capsules with Gauze		
19	3–4	6	4800	800
12	4–5	8	5600	700
5	5–6	10	6500	650
		Multiple Capsules with Introducer		
7	3–4	10	4800	480
2	4–5	12	4800	400

With the exception of those in whom tandems were used the patients have been grouped according to the depth of the uterus. With increase in uterine depth there can be seen increase in the number of sources used and total doses employed. For multiple capsules there has been a marked decrease in dose contributed per source.

So far as possible radium treatment has been followed by hysterectomy. The gross specimen obtained at operation supplies excellent material for studying the effect of irradiation. Among those in whom radical surgery could not be done the attempt has been made to evaluate treatment by means of curettement done at varying periods after complete irradiation. In a good many instances no additional procedure has been performed. Many of these patients had advanced lesions, and several are now dead. Others have refused examination by curettement. Evaluation of the group in whom no additional procedure has been done must wait for analysis of five year results. In Table II can be seen the incidence of persistent tumor as determined by hysterectomy or curettement. Among patients treated by intra-uterine tandems there were 16 followed by one of the above procedures. Residual tumor was found in

TABLE II

COMPARISON OF THE INCIDENCE OF PERSISTENT TUMOR FOUND AT HYSTERECTOMY OR BY CURETTEMENT IN CASES TREATED BY THE TWO DIFFERENT METHODS FOR APPLYING RADIUM

Procedure	Number of Cases	Residual Tumor	No Tumor Found	Approximate Percentage without Tumor
	Intra-uterine Tandem			
Hysterectomy	8	7	1	
Curettement	8	7	1	
None	8			
Total	24	14	2	15
	Multiple Capsules			
Hysterectomy	18	3	15	
Curettement	11	3	8	
None	16			
Total	45	6	23	80

all except two. Upon that basis cancer was destroyed by irradiation in only about 15 per cent. Among those treated by means of multiple capsules there are 18 upon whom hysterectomy has been performed. Residual tumor was found in only three. Curettement was done in 11 others, with residual tumor found in three. It should be noted that, among 29 patients treated with multiple capsules followed by hysterectomy or curettement, no residual tumor was identified in 23, or about 80 per cent.

Healy and Brown[8] have reported that histologic examination of uteri removed after treatment with an intra-uterine tandem revealed persistent carcinoma in possibly 1 out of every 3 patients. The residual tumor was often degenerated markedly, and appeared to be unviable. The authors noted that uteri of larger size were more apt to show persistent cancer, and concluded that enlargement of the uterus presented a more serious prognosis.

The presence or absence of identifiable carcinoma persisting in a uterus removed after preoperative irradiation does not provide a positive index as to the clinical result to be expected. Failures may occur among those showing no evidence of cancer due to the survival of some tumor cells in tissues not removed surgically. It can also be stated that those showing an abundance of persistent cancer will be cured if all the tumor is limited to the uterus itself. Donovan and Warren[6] have questioned the value of preoperative irradiation upon the basis of the high incidence of persistent cancer found in specimens obtained at hysterectomy. In the patients here reported the incidence is high among those treated with tandems, but remarkably low among those in whom multiple capsules were used. It should be noted that, in most clinical and statistical reports that have been published, the intra-uterine tandem has been the method generally employed for applying preoperative radium. The use of multiple capsules has made practical the administration of greater amounts of radiation. It is reasonable to believe, therefore, that the technique in question will, for several reasons, result in some improvement in clinical results. The margin of improvement is not expected to be great. It will apply chiefly to the occasional patient with moderate involvement of tissues adjacent to the uterus not removed surgically. The volume of tissue treated adequately by an intra-uterine tandem is not great. The use of multiple capsules will, due to the greater doses that can be employed, result in some increase in the volume of tissue receiving an adequate dose.

Table III

Persistence of cancer in specimens obtained by hysterectomy at different intervals after treatment by multiple tubes of radium introduced into the uterus

Time after Radium	Number of Cases	Residual Tumor	No Tumor Found
1 week	3	0	3
2 weeks	4	1	3
8 weeks	4	1	3
Over 8 weeks	7	1	6
	18	3	15

In the attempt to combine preoperative irradiation with surgery in the treatment of operable cases there must be an optimum time for hysterectomy. If the tumor is not destroyed completely there is every reason to believe that the uterus should be removed before recovery of inadequately treated carcinoma has occurred. Evidence of tumor recovery can be found occasionally in uteri showing persistent carcinoma. Those specimens are usually the ones removed about six weeks after radium treatment. The presence of tumor showing irradiation effect adjacent to areas of fully viable and actively growing carcinoma was interpreted as evidence of recovery in a study of regression of cervical cancer.[3] It is well within the limits of probabilities that corpus cancer might be expected to show evidence of recovery within six weeks. For that reason one may assume that, whenever practical, hysterectomy should be done before that period has elapsed.

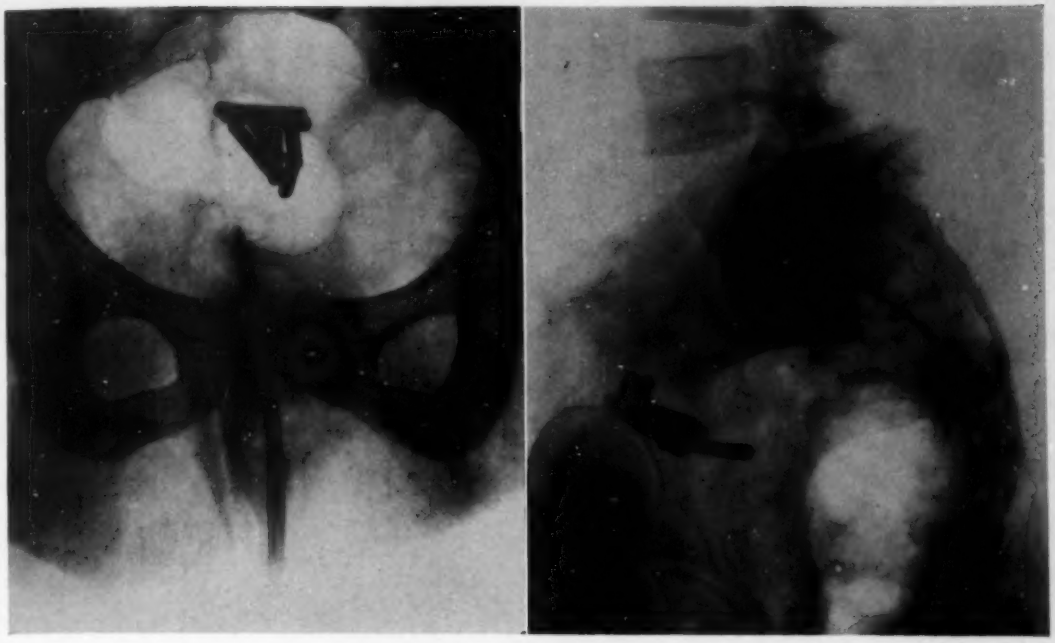

Fig. 3. Multiple sources of radium within a uterus of average size presenting no marked irregularities. Capsules in the fundus are lying transversely to the axis of the uterus.

In the attempt to better evaluate the optimum time for hysterectomy the interval between radium treatment and removal of the uterus has been varied deliberately. The results obtained in this experiment are given in Table III. It is significant that an absence of residual tumor has been noted in specimens removed as early as one week after radium treatment. No definite commitment can be made upon the optimum time for operation, but on the basis of tumor recovery there is evidence that surgery should be employed before six weeks has elapsed.

Each patient treated with multiple capsules has been studied by means of a roentgenogram taken while radium was in place. This procedure has been of value in the attempt to improve the technique. In Figure 3 can be seen an anteroposterior and lateral view made of a patient after multiple capsules had been introduced into the uterus. In the fundus the sources are lying transversely to the axis of the uterus. An arrangement of this sort produces a more uniform radiation effect, but is not easily obtained in every instance. Use of the shortest sources increases the possibility for placing tubes in that position. Another roentgenogram shown in Figure 4 illustrates the use of sources of greater diameter in the cervical canal. By this means the canal is kept sufficiently dilated for easy removal of the remaining tubes. It should be noted again that, among patients in whom the cervix is involved by a downgrowth of cancer, the intracervical capsule should be of greater strength, and radium should also be applied in the vagina.

Roentgenograms of a third case are shown in Figure 5. There are no capsules lying transversely across the fundus, and a tube of greater diameter was not used in the cervix. The roentgenograms are shown, however, for reasons of continuity. The uterus was removed two weeks after radium treatment. Two views of the gross specimen obtained at hysterectomy are shown in Figure 6. Upon opening the uterus the cavity presented a shaggy lining that could be stripped away with ease leaving a smooth, glistening surface except in the region of the fundus. The upper uterus probably received a lesser dose than more

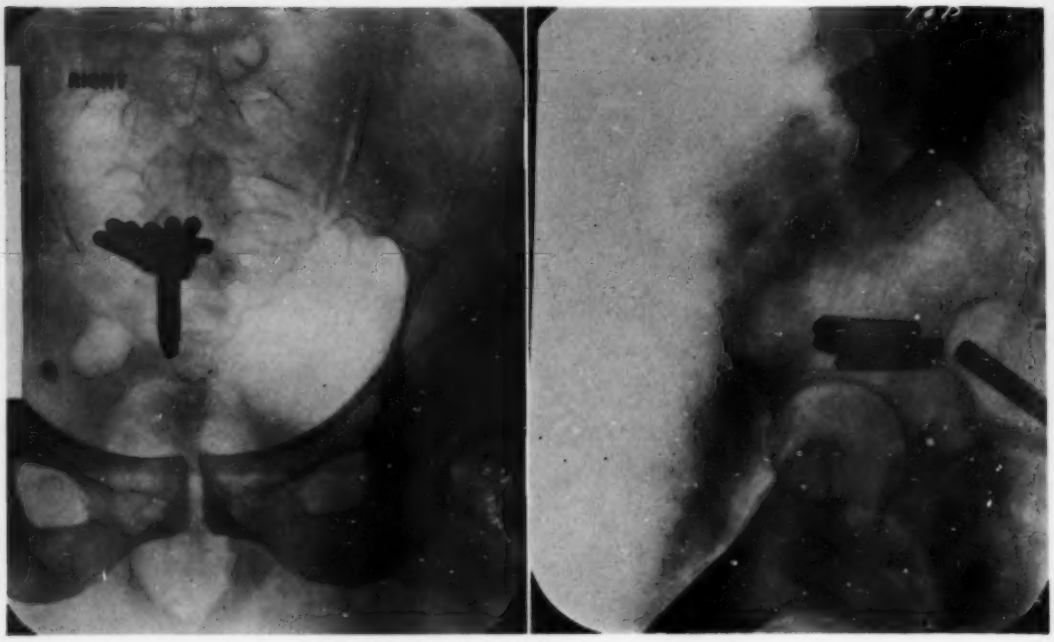

Fig. 4. Multiple sources of radium within a uterus somewhat larger than average. A capsule of greater external diameter is located in the cervix. By that means the canal is kept dilated for safe removal of the deeper tubes. The source in the cervix is of greater radium strength than those in the upper part of the uterus.

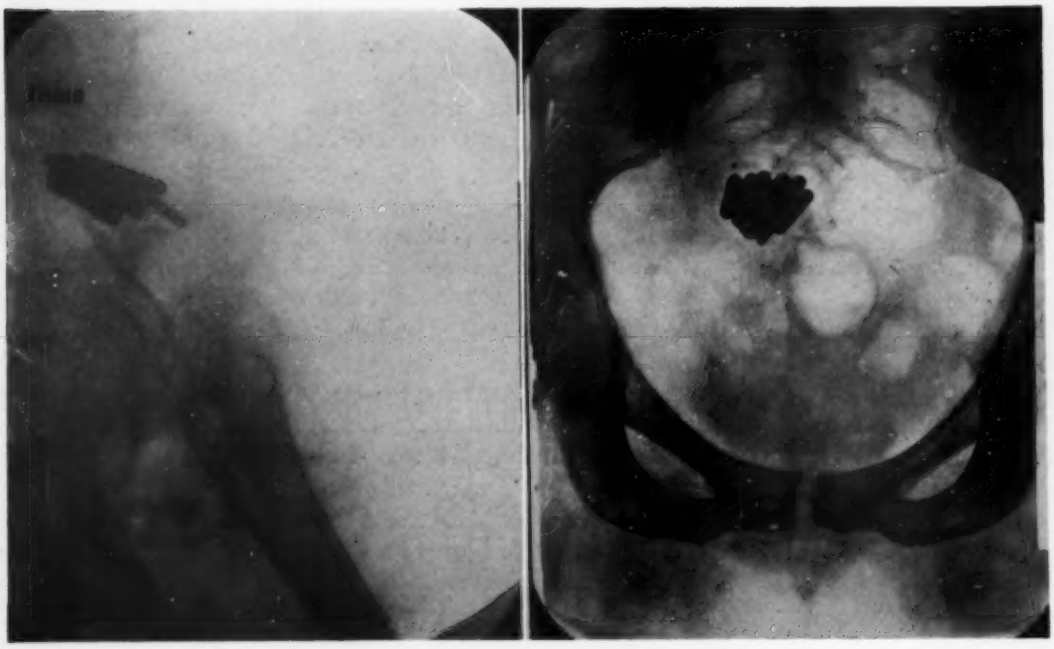

Fig. 5. Lateral and anteroposterior roentgenograms illustrating the radium treatment of a case operated upon two weeks later. The gross specimen is shown in Figure 6.

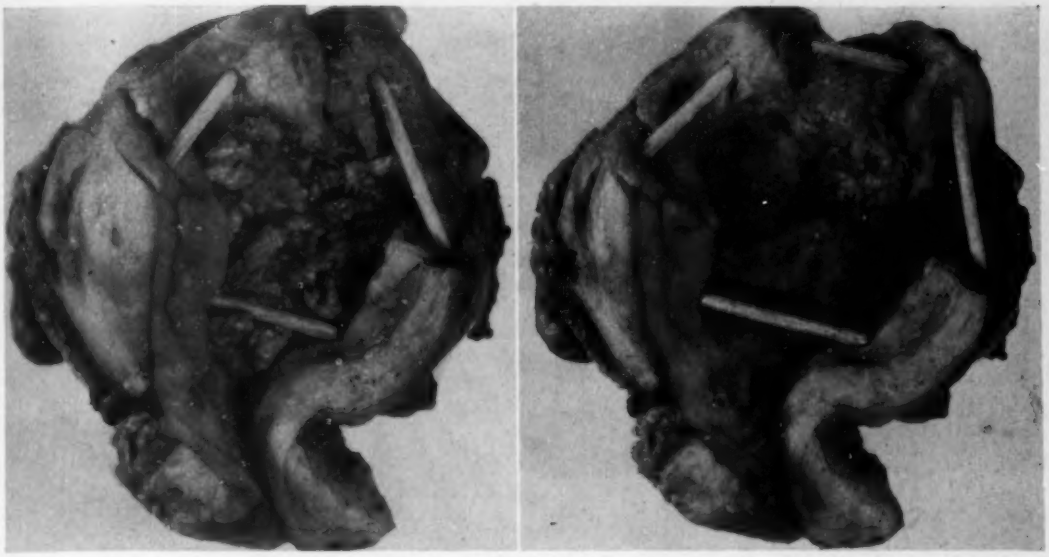

Fig. 6. Uterus removed from a patient two weeks after radium treatment shown roentgenographically in Figure 5. Superficial lesion presenting a degenerated and shaggy endometrial lining that was easily pulled away except in the fundus. Adherence in the upper uterus may be associated with a lesser dose falling in that region.

central regions. The finding of such a loosely attached endometrium is not unusual, but occurs chiefly in the more superficial types of lesions. Evidence of the lack of infiltration can be seen in the photomicrograph shown in Figure 7. This specimen was taken from a region where the lining of the cavity had been stripped away

Histologic examination of such degenerated endometrium has rarely shown viable cancer. Few cellular elements remain, and the endometrium is replaced chiefly by exudate. The exudate undergoes gradual organization, as can be seen in Figure 8.

Fig. 7. Photomicrograph taken from the uterus shown in Figure 6, and illustrating the lack of infiltration. Section is from a part of the uterus from which the endometrial lining was pulled away.

Fig. 8. Photomicrograph showing well developed organization of the inflammatory exudate replacing endometrium, and presumably tumor, in a uterus removed six weeks after radium treatment. Section from near fundus.

Fig. 9. Photomicrograph taken from near the cervix of the same specimen as shown in Figure 8, and showing the absence of necrosis and marked uniformity of irradiation effect at the two extremes of the uterus.

The section was taken from a uterus removed six weeks after radium treatment. Organization of the inflammatory exudate has taken place, and there is a beginning single layered growth of epithelium on the surface forming a new lining for the uterine cavity. This particular uterus showed a remarkable uniformity of radiation effect so far as histologic changes were concerned. The section already described was obtained from the fundus. A photomicrograph of tissue from the cervix is shown in Figure 9. Both of these sections show destruction of epithelial cells without residual necrosis. In each there is a comparable degree of injury to muscle and connective tissue as well as blood vessels. Such a uniform distribution of radiation effect is not obtained in all patients treated with multiple capsules, however, as can be seen in Figure 10. There is no question as to the presence of viable carcinoma in this specimen removed two weeks after radium was applied. There were, however, some areas in which complete degeneration of tumor had occurred.

There is one case for whom particular discussion is indicated. Roentgenograms taken during radium treatment revealed an atypical arrangement of intra-uterine sources. In both the anteroposterior and lateral views shown in Figure 11 there is evidence that two capsules are outside the uterine cavity. The presence of fever gave additional evidence that the uterus was perforated, and for that reason the radium was removed. One week later a second radium treatment was given without untoward effects. Hysterectomy was done several days afterward. At operation the point of perforation was found extending into a small abscess buried in dense adhesions between the uterus and sigmoid colon. There was no residual tumor found in the gross specimen, and the patient made a satisfactory recovery. Follow-up has extended over a period of nine months without evidence of recurrence. About three months after hysterectomy, however, the patient was re-admitted to Barnes Hospital with symptoms of partial intestinal obstruction. These symptoms subsided under conservative treatment, and no other sequelae have occurred.

It is interesting to note that Heyman, Reuterwall and Benner[10] report a similar experience. In their presentation was published a photograph in which a similar arrangement of intra-uterine sources was

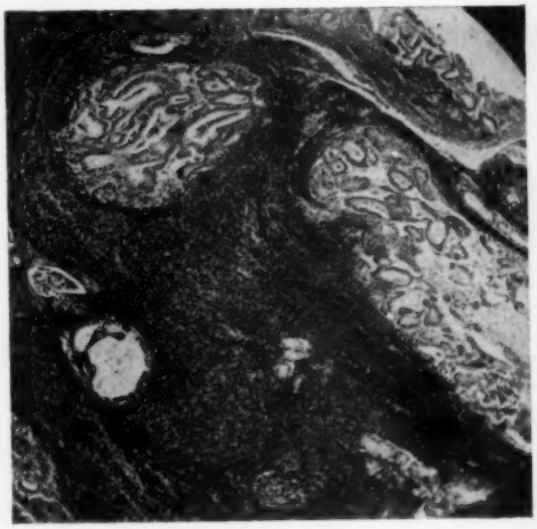

Fig. 10. Photomicrograph showing the persistence of cancer in a uterus removed two weeks after radium treatment.

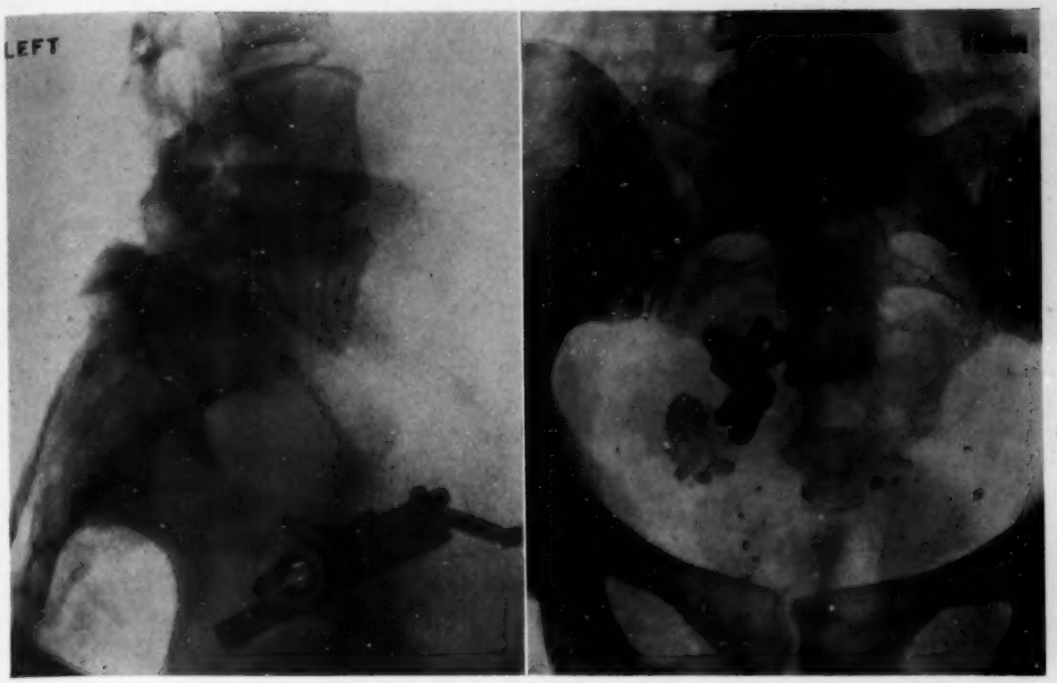

Fig. 11. Roentgenograms showing an atypical arrangement of intra-uterine sources of radium indicating a perforation of the uterine wall.

found. Such instances illustrate clearly the value of roentgenograms taken during each treatment. Perforation of the uterus may present serious complications. It should be noted, however, that only one such injury is known to have occurred in our series of more than 45 cases of corpus cancer treated with multiple capsules. It is to be hoped that some time will elapse before such an accident occurs again, but one cannot expect always to avoid perforation, even in the simplest types of intra-uterine procedure. If in radium treatment there is a greater risk of perforation with multiple capsules, the better irradiation effects obtained by the method would seem to offset the added risk incurred.

Any improvement in clinical results following the addition of irradiation to the treatment of operable patients must be due to an effect upon tumor cells outside the volume of tissue removed surgically. In corpus cancer the point arises immediately as to how often there is apt to be extension outside the uterus itself. This cannot be determined on the basis of the histologic grade of the lesion, and it is impossible to visualize or adequately palpate such extensions. The occasional patient with local recurrence after hysterectomy alone is, however, proof that involvement of those regions does occur. It seems logical, therefore, to employ both irradiation and hysterectomy in all operable patients. At the same time it is difficult to reconcile the use of a large amount of radiation followed promptly by complete removal of the uterus. There can be no doubt that the greater tissue dose obtained outside the uterus by combining roentgen rays with radium before hysterectomy is responsible in part for the relative superiority for preoperative treatment over postoperative roentgen irradiation alone. It should be noted, however, that in most instances the dose falling on tissues outside the uterus is not great. It would seem that there must be other factors responsible for the greater effectiveness of preoperative treatment. An explanation can be attempted upon the

basis of biologic factors. One might expect a greater degree of radiosensitivity before hysterectomy. Following removal of the uterus there is production of fibrosis, interference with vascular supply, and disturbed anatomical relationships. Those factors might contribute to greater radioresistance, and thereby decrease the effectiveness of the relatively small amounts of postoperative radiation falling on regions not removed surgically. It would not seem that hysterectomy would interfere materially with the effect of radiation already applied to the outlying tissues. In fact the reverse might be true, in that the results from surgery actually augment the effectiveness of the previous treatment.

In planning preoperative treatment the use of both roentgen rays and radium is to be recommended. The greater tumor dose obtained by a combination of the two methods is not the only indication for following such a program. For corpus cancer there are advantages gained in beginning treatment with roentgen rays that are identical in some respects to those noted in cervical carcinomas. Infection present in the lesion is decreased by preliminary roentgen irradiation. As a result of the decrease in infection there is less risk of necrosis from radium, and possibly a more favorable degree of radiosensitivity. In addition the effects of roentgen irradiation should lessen the risk of perforation in the more infiltrating types of lesions, and decrease the risk of radium capsules acting as pistons to force viable cancer cells through the lumina of the tubes in all cases.

It is obvious that any advance in methods of treatment for corpus cancer will improve clinical results not only in operable patients, but also in those unsuited to hysterectomy. So far as radium treatment is concerned, therefore, it can be said we are faced with a double responsibility. It is first necessary to devise a technique of treatment that will deliver a more practical distribution of radiation than that which is obtained from the usual intra-uterine tandem. By that means one may expect an improvement in results among cases not suited to hysterectomy due to advanced involvement or some associated constitutional disorder. The second responsibility rests upon the more widespread application of improved radium technique to operable cases.

SUMMARY AND CONCLUSIONS

In 1938 the attempt was made to improve the effectiveness of radium treatment employed for cancer of the corpus uteri at the Barnard Free Skin and Cancer Hospital, and on the teaching service of the Barnes Hospital. A technique employing multiple sources of radium within the uterus was employed. Several modifications have been made in the attempt to simulate the method employed by Heyman. The technique is described, but sufficient time has not elapsed to permit a statistical summary upon the results obtained. The number of patients treated is believed adequate, however, for a preliminary report upon the method in use.

Each case has been studied by means of roentgenograms taken while radium was in situ. The effect of irradiation upon the local lesion has been studied in gross specimens obtained at hysterectomy, or by curettement, whenever possible, in cases not suited to surgery. A marked decrease in the incidence of persistent carcinoma is noted for the multiple capsule technique in comparison with patients treated in the same clinics with an intra-uterine tandem containing radium. For the multiple-capsule method there has been an increase in the total amount of radiation employed, but a marked decrease in the dose contributed by each individual source. As a result there has been a lesser amount of necrosis and other sequelae.

The presence or absence of persistent cancer in a previously irradiated uterus cannot be interpreted as an accurate index of the end-result to be expected. Due to the marked improvement in irradiation effect noted for multiple capsules, however, it is believed that an improvement in clinical results is to be expected.

The value of preoperative irradiation is discussed, and for operable cases it is recommended that hysterectomy be preceded by preliminary roentgen irradiation and radium applied within the uterus. A multiple-capsule technique is advocated for the intra-uterine radium treatment of both operable and inoperable patients. The uterus is known to have been perforated in one instance. Experience with that patient is described briefly.

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DISCUSSION OF PAPERS BY DRS. BOWING AND FRICKE, MARTIN, AND NOLAN AND ARNESON

Dr. Maurice Lenz, New York. Drs. Bowing and Fricke have shown that prognosis in cancer of the fundus and cervix depends on the clinical stage of the cancer, at the time of treatment. Results of hysterectomy, the use of which is limited to Stages I and II, therefore cannot be compared with the results of radiotherapy, which, besides Stages I and II includes Stages III and IV.

In radiation treatment of cancer of the cervix, the clinical stage was practically the only factor which determined the outcome of the treatment. In irradiated cancer of the fundus, on the other hand, microscopic grading also influenced prognosis. In this connection, it should be borne in mind that clinical classification, as to the extent of the tumor, is less accurate in cancer of the fundus than in cancer of the cervix. In cancer of the fundus, therefore, it is more likely that more of clinical Stage IV cancers will be mistakenly classified as less extensive stages, than in cancer of the cervix. The majority of the extensive fundus cancers probably fit into the less differentiated groups. The same may be said of the cervix. Intensive and more adequate irradiation of the entire pelvis, however, is more commonly carried out in cancer of the cervix than in cancer of the fundus. The grave influence of anaplasia in cancer of the cervix is illustrated by the surgical results in this disease.

Dr. Martin has emphasized the importance of avoiding over-irradiation of the intestine and bladder when irradiating cancer of the cervix. In addition to burns due to gross physical causes, such as overcrossing of roentgen-ray beams and misplacement of radium tubes,

there may be physiological reasons for injuries of adjacent structures, as e.g., when seeds or needles are repeatedly inserted into poorly vascularized vaginal septa or when a large amount of roentgen radiation or radium is administered in a short time; the rectum and bladder do not support intensive short treatment as readily as when the same quantity of radiation is delivered in a longer period of time. The report of the Standardization Committee of the American Radium Society in 1937 called special attention to this possible source of injury, basing its conclusions on a survey of 2,855 radiation treated cancers of the cervix. As a result of this survey, the period of the intracavitary radium therapy at the Presbyterian Hospital, New York, was raised from forty to one hundred hours, and the period of the roentgen treatments was lengthened from twenty to forty or even sixty days, while retaining the same total radiation doses. Since then, practically no bladder or intestinal injuries have been seen at the Presbyterian Hospital.

In spite of the danger of irradiation injury in radiotherapy of cancer of the cervix, the importance of roentgen treatment should not be underestimated, even in cases which clinically are classified as Stages I and II. Clinical determination of the extent of the cancer is not very accurate, and intracavitary radium does not adequately irradiate silent parametrial extensions and regional lymph node metastases. While the roentgen-ray dosage which may be administered safely is probably sufficient only to restrain such growths and not to destroy them, even this effect may prolong life.

Drs. Arneson and Nolan clearly demonstrated that in the radium treatment of cancer of the fundus in large uteri, Heyman's method of filling the uterus with multiple radium tubes is superior to the use of single, "Y" shaped, or triple, radium-containing applicators. Adequate intra-uterine irradiation in fundus cancer is important especially in very fat women, as in them it is difficult to deliver a satisfactory depth dose with external 200 kv. roentgen therapy.

Dr. Milton Friedman, New York. I would like to discuss two points: first, there is no question that in the treatment of carcinoma of the cervix the addition of roentgen therapy to radium therapy improves the results. Under certain ideal circumstances (a radiosensitive tumor in a thin patient), the daily tumor dose and the total dose may be such that roentgen therapy alone can eradicate the tumor.

Under different circumstances, pre-radium roentgen therapy can unfavorably affect the outcome. In obese patients, the daily tumor dose is inadequately small, being in the neighborhood of 100 r. When such irradiation is carried on for four or five weeks, and then another week or two elapses while the patient is being admitted to the hospital and prepared for operation, there may be a total lapse of time of five to seven weeks between the first roentgen treatment and the radium insertion. As a result, only the more radiosensitive tumor cells are destroyed; the remaining cells mature and become more radioresistant; the tumor bed becomes more fibrous and less vascular; and consequently it becomes necessary to administer a very large dose of radium to a tumor which is now more radioresistant, and which lies in a tumor bed that is now less tolerant to radiation. This was strikingly illustrated in a series of patients who received preliminary roentgen therapy of 3,000 to 4,000 r to each of four skin portals over a period of five weeks, and then 7,000 to 8,000 mg-hr. radium (Curie technique). To our amazement, one-fourth of the patients developed local recurrences in the cervix itself.

The solution is varied, depending upon the radiosensitivity of the tumor, the skin-tumor distance, and the daily tumor dose. The arrest of carcinoma of the cervix is accomplished essentially with radium. Roentgen therapy is an adjuvant which offers variable though limited assistance.

Another point: There appear to be as many corpus carcinoma radium gadgeteers as there are military armchair strategists. The principles of multiple foci of radium, and flexibility of their dispersion are essential. When multiple tubes are used, it is necessary to fix them in position, otherwise they will drop to the dependent part of the uterus, and will leave the fundus and upper corpus under-irradiated. At least one tube should rest broadside against the fundus. Little radiation comes from the end of a radium tube. Several tandems situated more or less vertically in the uterus will not effectively irradiate the fundus and the cornua.

Dr. Bowing (closing). As to Dr. Lenz's reference to the statistical phase of my paper, I am sorry that I do not feel qualified to enter upon a worthwhile discussion of the probable values contained in statistical data, and the

best or most suitable method of calculating the end-results in the treatment of cancer of the uterus. I am most certain the Division of Biometry and Medical Statistics at the Mayo Clinic would be glad to provide a discussion of our methods of calculation and presentation of statistical material. I shall be pleased to help in every way I can.

The point which Dr. Lenz wishes to make in his statement that all Grade 4 lesions, if studied would be found to be inoperable because of their extent alone is not clear to me. In the main, his statement is acceptable; however, it seems possible that in some cases a lesion of Stage I or II could have a Grade 4 pathologic change or category. In other words, Dr. Broders' early studies concerning the estimation of grade were carried out on surgical material. When grade alone was considered, 90 per cent of those patients who had Grade 4 lesions did poorly after surgical intervention. Studies are in progress which will show the relationship between grade and stage of involvement and the surgical results obtained.

The influence of the age of the patient and the grade of the lesion is of interest. On the basis of our limited studies of cases of cancer of the uterine cervix, we may conclude that age does not affect grade in that the young adult patient may have malignant lesions of any one of the four grades. There seems to be no predominance of particular observations in the group studied.

The point I wish to emphasize is that the gross characteristics and extent of a lesion of the uterine cervix are, in the main, the deciding factors governing the initial application of radium. In other words, the treatment is not administered with only the grade of the lesion as the determining factor. Furthermore, it is important to space applications of radium so that local necrosis or enhancement of the local necrosis already present will be avoided, and so that regional and systemic reactions will be reduced to a minimum. In brief, the importance of individualized radium therapy is recognized.

We rather expected the results obtained in the treatment of cancer of the body of the uterus, because the radium treatment of that particular condition can be classed as a standard technique, devoid of many valuable individual factors. Therefore, our results should be rather uniform for comparisons.

Dr. Friedman mentioned the fact that many different types of radium applicators have been designed for intra-uterine treatment, although my experience with the various types is rather small. Yet, I am of the opinion that as a rule they all possess common factors governing their limitations in intra-uterine treatment.

In answer to the inquiry concerning the use of preliminary roentgen treatment in our cases of cancer of the uterine cervix, I can say that we do not employ this method routinely. We do have in our files records of a small number of patients so treated, as well as records of a larger number of patients who came to our section for further consideration after preliminary roentgen treatment had been administered elsewhere. On the basis of these observations and our own experience, we believe that the rather prompt beneficial response obtained by the initial application of radium produces a superior early result, and that, also, the economic or time factor involved in the technique of preliminary roentgen treatment is greater than it is in our procedure of initial radium therapy followed by supplemental roentgen therapy. I feel rather certain that there is as yet no substitute for the well-planned technique of initial treatment with radium for patients who have cancer of the uterine cervix.

I agree with Dr. Martin's statement that maintenance of the integrity of the tissues which compose the tumor bed is very essential for satisfactory early and late results of treatment. The selection of the proper treatment factors for each patient will make the convalescence shorter and reduce to a minimum the probable late, painful and disabling sequelae. This feature of any technique of treatment is worthy of all possible attention.

Preoperative irradiation was also mentioned. This is a very interesting method of treatment and is deserving of consideration. Briefly, preoperative treatment is applied today in a very limited way. The few patients we have treated were treated by various techniques. Satisfactory statistical studies are not available. Evidently, some definite good can be expected from the procedure. A suitable preoperative technique remains to be established. Certain features seem important. For example, (1) the treatment should be administered with the thought in mind that other therapeutic procedures will follow; (2) the time allowed between this type of treatment and surgical intervention should be sufficient to permit the

utmost good to result from the therapeutic effects and to permit tissue reactions to subside, and this interval probably is a matter of weeks or in some cases months, and (3) it should not be expected that inoperable lesions will be made operable by means of preoperative treatment. In the future this method of treatment may become more favored than it is today. In some communities an economic factor may limit general acceptance of it.

Dr. Martin (closing). I wish to thank Dr. Lenz for his excellent discussion and to apologize for not stressing his report made in 1937. Apparently his experience more or less parallels ours. The numerous reports of serious injuries which have appeared in medical journals during the past few years indicate that his work has been disregarded in many quarters.

I will be much interested in his final survival rate in Stage III cases treated with his intensive roentgen-ray technique without serious sequelae. Most of the reports which I have studied have not shown enough improvement in five year survival rate from the more intensive techniques to convince me that the increased danger to normal structures is justifiable.

Dr. Lenz stated that intensive preliminary roentgen therapy makes the application of radium easier. In our experience such has not been the case. This is probably due to the fact that we like to use large radium spools in the vaginal vaults and the shrinkage resulting from the roentgen irradiation makes their proper application practically impossible.

In going over the literature I have been unable to find any accurate experimental data covering the exact tolerance doses for the normal structures in the pelvis under standard treatment conditions. In my opinion, some of the research departments in our large institutions should be put to work on this important problem.

Since I also have devised a radium applicator for the treatment of cancer of the uterine fundus, I cannot resist the temptation to discuss that subject. The multiple capsules advocated by Heyman are only effective when they are kept well up in the top of the uterus in intimate contact with the malignant tissue. If they are held in place by a pack, drainage is interfered with and when they are not packed in position they tend to fall away from the tumor. Each of our capsules is attached to a short wire by a hinge. A loop on the lower end of each wire protrudes through the external os and when the fundus is filled with capsules drainage is maintained along the wires which insure their being held in the proper position. The hinges allow the capsules to be maneuvered into uterine cavities of various shapes and sizes. It seems reasonable to assume that Dr. Healy's prognostic sign, namely, the size of the uterus may no longer be so important when the larger tumors are more efficiently irradiated.

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CANCER OF THE CERVIX

THE EFFECT ON THE RATE OF CURE OF INCREASED ROENTGEN RADIATION TO THE PARAMETRIA*

By WILLIAM P. HEALY, M.D., *and* GRAY H. TWOMBLY, M.D.
From the Memorial Hospital
NEW YORK, NEW YORK

IN THE six years from 1932 to 1937, nine hundred and twenty cases of primary cancer of the cervix were seen in the gynecological department of the Memorial Hospital. This total is large. The patients have been seen and treated by a few men. During this period the method of giving radium has been practically constant while several different schemes of giving external roentgen therapy have been used. Consequently, this group of cases offers an almost ideal set of statistics for an inquiry into the question of what value roentgen therapy may have in the treatment of cancer of the cervix and what form of roentgen therapy appears to be the most effective.

In 1931 Healy[4] reviewed the results of treatment of 1,574 cases of carcinoma of the cervix at the Memorial Hospital. This included all cases seen and treated from 1918 up to 1931. During this period the treatment given consisted of a vaginal bomb for 1,000–3,000 mc-hr. with a filtration of 2 mm. of brass, and an application of radium to the cervical canal of 1,500 to 3,000 mc-hr. filtered with 0.5 mm. of platinum or gold and 1 mm. of rubber. In addition, from 1918 to 1925, unfiltered glass radon seeds for 200 to 2,000 mc-hr. were inserted into the cervix. In 1925 these were replaced with gold seeds, 0.3 mm. in wall thickness.

External irradiation was given from 1918 to 1921 with radium in an external pack in six positions around the pelvis. The radium was held on a brass and bakelite block 4 cm. away from the skin and a total dose of 9,000 to 18,000 mc-hr. given. In 1922 this was replaced by low voltage roentgen radiation with 4 mm. of aluminum filtration delivered at a target-skin distance of .30 cm.; 140 kv. (peak). Sixty ma-min. or about 400 r were delivered to each of four fields. The roentgen as a unit of roentgen-ray measurement had not been established at this time. This dose is estimated on the basis of the skin reactions usually observed. In 1926 this type of treatment was replaced by high voltage roentgen therapy.

As we know now, the amount of radiation delivered to the cervix or parametria by the external radiation therapy used from 1918 to 1926 was not very large. Consequently, the five year cure rate reported by Healy of 22.5 per cent represents what may be expected by the application of radium alone to the cervix as we have continued to use it, for the dose of radium used in our cases up to and including 1937 is essentially unchanged from that reported in this paper of Healy's.

In 1937 Healy and Frazell[7] reported the results of treatment of 551 cases of primary carcinoma of the cervix seen during the years 1928 to 1931, inclusive. These patients were treated first with high voltage external roentgen therapy delivered through four 10 by 15 cm. pelvic portals. The daily dose was 750 r to one field. The physical factors were 200 kv. (peak), 4 or 30 ma., 50 cm. target-skin distance, and 0.5 mm. Cu filtration. Within a week or ten days following the last roentgen treatment, a radium treatment of 1,500 mc-hr. was given directly against the cervix by means of a vaginal applicator or "bomb." The following day an intracervical and intra-uterine application of radium of 3,000 mc-hr. was made with two capsules, the filtration of which was 0.5 mm. platinum and 1 mm. rubber.

The five year survival rate for this

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method of treatment in this group of cases was found to be 27.7 per cent. These figures suggest that the addition of more efficient high voltage external roentgen therapy previous to the local application of radium had raised the cure rate approximately 23 per cent.

In 1934 Arneson and Quimby[2] reported a study of the distribution of roentgen radiation within the female pelvis for different physical factors of irradiation. They concluded that the use of six pelvic fields, each 10 by 15 cm. (two anterior, two posterior, and one on each lateral surface) with a target-skin distance of 70 cm. was the most desirable of the methods they investigated for giving external irradiation in cancer of the cervix. While this report was published in 1935, the studies which led up to it had been made several years previously and the treatment in favorable cases in our clinic had been changed in 1933 by using six fields, increasing the distance to 70 cm. and giving daily doses to each of two fields of 200 r. The total dose per field was 2,000 to 2,400 r. Again the physical factors were 200 kv. (peak), 30 ma. current, 0.5 mm. Cu and 2 mm. Al filtration. This treatment took three to four weeks to complete. It was estimated that it delivered 3 to 5 threshold erythema doses to the parametria for a distance of 10 to 11 cm. lateral to the cervical canal. This method of treating patients was reported first by Healy and Arneson[6] in September, 1933 (see Fig. 1).

In 1935 Healy[5] made a preliminary report on 107 patients who had been so treated. He found skin reactions and intestinal disturbances more marked than with single doses of 700 r to each of six fields. Rarely were the skin reactions severe enough to force the stopping or postponing of the treatment, but occasionally the symptoms of large bowel irritation did so. Bladder symptoms were found to be mild. The immediate healing observed in the cervix and the marked regressive changes observed microscopically in the tumor, while not complete, were exceedingly encouraging.

This method of treating cancer of the cervix was continued for several years and will be referred to as "divided dose technique" in this paper. It was used routinely on clinic patients from 1933 to 1936 when the patient lived near the hospital so that daily visits were practical for her.

In private cases, largely for economic reasons, treatment through four or six pelvic portals with doses of 700 to 750 r to each portal were continued throughout this period. Patients living at a distance were also so treated. This method will be referred to as "massive dose technique."

It should be noted, as shown in Figure 1, that the total amount of roentgen radiation delivered to the parametria in the "divided dose" type of treatment is much greater than that given by the "massive dose" type. The tissues lying next to the walls of the pelvis receive less than one threshold erythema dose of radiation when a radium bomb and tandem alone are used. With the "massive dose" type of treatment these tissues receive 0.8 to 2 threshold erythema doses. When the "divided dose" technique is used and 12×200 r (2,400 r) is delivered at 70 cm. to each of six fields, the same areas receive 4 to 7 threshold erythema doses. Of course, it must be remembered that "massive dose" technique requires only a week or less to deliver the full dose, while "divided dose" therapy usually requires thirty-six treatment days or six weeks. Thus, the increase in dose to the parametria is probably less than arithmetical if one considers the factor of biological recovery taking place in such a treatment interval.

In his report in 1935 Healy[5] notes observations made by Stewart on multiple biopsies taken from the cervix during the course of "divided dose" roentgen therapy. Stewart felt that in some instances the later biopsies showed a slowing up in irradiation effect on the cancer cells after a week or ten days of treatment. Following this lead 14 cases were treated through four portals giving 200 r×5 to each portal, or a total of 1,000 r, and then increasing the daily

dose to 300 r for five additional treatments to each portal. This gave a total dose of 2,500 r. Two cases were given 200 r for one cycle, 300 r for four cycles, and 400 r for three cycles, or 2,600 r per portal. Another

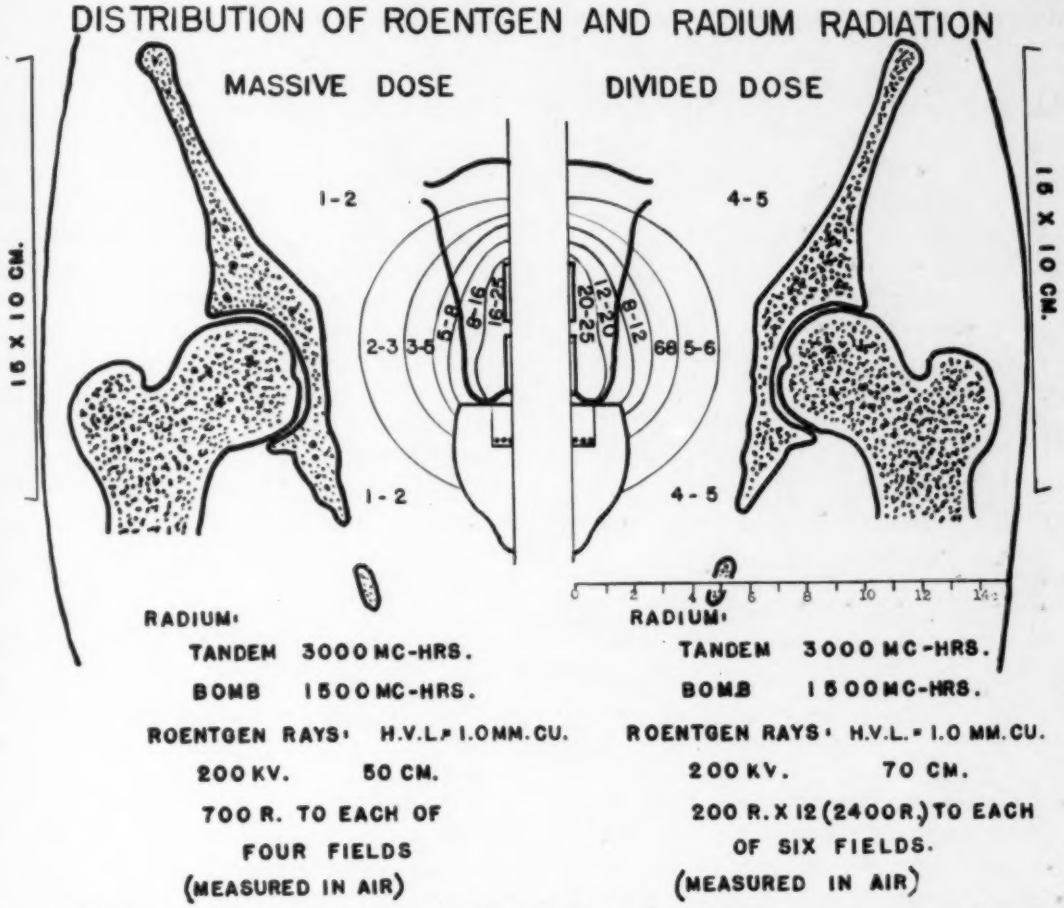

FIG. 1. A diagram to show the distribution of radiation in the average female pelvis when the radium dosage is kept constant (bomb with 1,500 mc-hr. Tandem = 2,000 mc-hr. in the lower capsule, 1,000 mc-hr. in the upper capsule) and the external roentgen therapy is varied. It should be noted that "massive dose" as pictured would take four days to deliver; "divided dose," thirty-six days, and this time interval is of biological importance (data for diagram taken from Arneson).[1]

method followed in some cases was to give 200 r×5 to each portal and follow with 250 r×2 or a total of 1,500 r to each of six portals. The groups so treated were small and all are included under the heading "divided dose technique."

In 1936, following the suggestions of Stewart about the apparent increasing radioresistance of cervical cancer during the course of roentgen therapy, a new technique was adopted and has been used on all ambulatory clinic cases living near the hospital up to the present time. This we will refer to as "pyramidal dose technique." It consists in treating the patient through six pelvic portals, each 10 by 15 cm., two anterior, two posterior, and one on each side. The factors are 200 kv. (peak), 0.5 mm. Cu filter, 30 ma. current, and 70 cm. target-skin distance. Two opposite portals are treated daily. These receive 100 r the first day. Two more receive 100 r the next day, and the last two 100 r on the third day. On the fourth day the first two portals receive 150 r, and so on. The third

cycle is 200 r per portal; the fourth, 250 r; the fifth, 300 r; the sixth, 350 r; and the seventh, 350 r. This totals 1,700 r per portal. This amount of roentgen radiation, with the factors given, seems, in the majority of the patients so treated, to represent the maximum dosage that the normal tissues in the irradiated fields can withstand. Moreover, at this dosage level many patients are inclined to develop marked digestive and intestinal disturbances. The entire treatment takes three and a half weeks. Four to six weeks later a vaginal applicator containing radium is inserted for 1,000 to 1,500 mc-hr. and the next day a radium tandem is placed in the cervical canal for 3,000 mc-hr. The filtration is 0.5 mm. platinum and 1 mm. rubber. Two tubes of radon are used, the upper, which goes into the uterine cavity, containing one-half the amount in the lower capsule while lies directly against the cancer in the cervix.

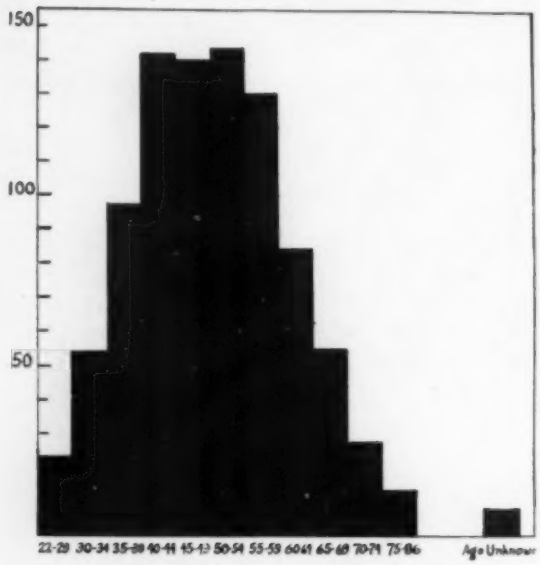

Fig. 2. Age distribution of 920 cases of primary carcinoma of the cervix seen at the Memorial Hospital between 1932 and 1937 inclusive.

As mentioned in our introductory paragraph, this method of applying radium has not changed from 1932 to the present. We have then, a large number of cases receiving the same dose of radium, seen by the same attending physicians, followed with the same care, and drawn from the same population, the only variable being the use of one of three methods of external roentgen therapy, i.e. "massive," "divided," or "pyramidal dose technique."

MATERIAL

During these years 920 cases of primary carcinoma of the cervix have been seen and treated in our clinic. The age distribution is given in Figure 2 which shows the highest incidence to lie between forty-five and forty-nine. Twenty-three cases were under thirty years of age; the youngest, twenty-two; thirteen were over seventy-five, the oldest being eighty-six.

The majority of cases occurred in married women who had borne children. Of the 920 patients, 607 were married and 240 widowed while 42 were separated or divorced. Only 24 were single and of these, 6 admitted that they had been pregnant or borne children. On 7 charts the marital status was not recorded. Thus, only 18 out of 913, or 2 per cent, were even nominally virgins. These figures serve to emphasize once again that cancer of the cervix is a disease of married and usually parous women.

Turning to the nationality of the patients, as indicated by the hospital records, it is found that 417, or 45.3 per cent, were born in the United States. Italians made up the next largest group with 126, or 13.7 per cent. There were 78 Negroes, or 8.5 per cent, 62 Germans, Dutch or Austrians, or 6.7 per cent, and 41 Irish, or 4.4 per cent. In spite of the large Jewish population in New York and the preponderance of Jews in our other clinics, only 46, or 5.0 per cent, were Jewish in this group suffering from cancer of the cervix. This figure is a generous one. There was no way of checking race save by the charts. If a name was Jewish but no special note was made of the patient's racial extraction, she was counted as Jewish. Consequently, the 46 probably include several who do not belong in this group. It is

indeed a striking fact that a maximum of only 5 per cent of the cases of cancer of the cervix occurred in Jewish women, and it is hard to believe that this can be accounted for by any marked difference in sexual hygiene. The occurrence of cancer in the cervix among married women with uncircumcised husbands would seem a fertile field for research into etiological relationships.

The possibility that the kind of partner may play a larger rôle than the parity of the patients is suggested further when one examines the reproductive histories of our patients. Of 532, in whom complete reproductive histories were recorded, 70, or 13.1 per cent, had never been pregnant. Many had been pregnant a large number of times, however, so that the average number of pregnancies was 4 per patient. The number of viable births in this group averaged 3.03 per patient.

Is there any abnormality about the menstrual history of patients who later develop cancer of the cervix? Our data are not complete, but what we have fail to show any striking features. Of 379 patients, 221 stated that the onset of their menstrual periods was between the ages of thirteen and fifteen. Ninety-four began to menstruate at the age of twelve or younger; 64 at sixteen or older. Of 413 patients, 390 menstruated every twenty-four to thirty-two days; 22 every twenty-three days or less and 1 every thirty-three days or longer.

TABLE I

DURATION OF SYMPTOMS

Length of Time	No. of Cases
Under 2 weeks	21
Between 2 weeks and 1 month	49
1 to 2 months	141
3 to 5 months	228
6 to 11 months	196
12 to 23 months	151
24 to 35 months	56
36 months or more	50
Not stated	28
TOTAL	920

The duration of flow was three to six days in 296 patients. It was prolonged to seven days or more in 54 and was scanty, lasting two days or less, in 19. Thirty-five patients said that ther periods were "irregular."

An attempt was made to determine whether any previous gynecological operations had been performed on many of the

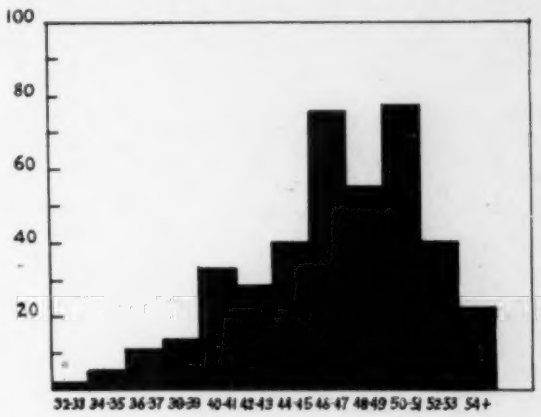

FIG. 3. Age at the menopause of 402 cases of cancer of the cervix.

patients but on this point not much information was recorded on the charts. Thirty-two patients said that they had undergone dilatation and curettage previous to the onset of the present illness. In 1 case the cervix had been cauterized. In 7 it had been repaired. Evidently the last type of operation will not prevent cancer of the cervix in all cases. In 24 patients some type of vaginal plastic operation had been done. Forty-eight had lost one or both ovaries.

In 383 the menopause had not been reached. The age distribution at the menopause in the remaining 402, in which this fact was recorded, is shown in Figure 3 with the highest incidence at forty-six to forty-seven and fifty to fifty-one.

Of course the commonest symptom of cancer of the cervix is bleeding. This was noted as occurring between the periods or after the menopause in 786 instances. Contact bleeding was noted by 138 patients; increased flow at the periods by 141; 449 had vaginal discharge; 331, pain; 294, loss of weight; while 18 had urinary inconti-

nence. In Table 1 is recorded the duration of symptoms. It is to be noted especially that 257 had been aware of some symptom for a year or more before they came to us. This is 27.9 per cent of the whole group. It constitutes an unfavorable commentary on our ability to get early treatment to the patient with this disease.

From these figures it is seen that our entire group of 920 cases are not very different from other groups having cancer

Table II

REASONS FOR UNSUITABILITY OF 351 CASES AS MATERIAL FOR THIS STUDY

1. No bomb or tandem used in this hospital	100
2. No bomb	75
3. No tandem	31
4. No primary roentgen therapy in this hospital but orthodox radium treatment	57
5. No primary roentgen therapy or bomb	14
6. No primary roentgen therapy or tandem	6
7. Roentgen therapy only partially completed	3
8. No roentgen or radium therapy in this hospital	40
9. No biopsy obtained	17
10. Patient followed for less than 1 month after completion of treatment	2
11. Mixed forms of roentgen therapy (i.e., part massive, part divided)	3
12. Radium given in some special manner	2
13. Rare tumor of the cervix—"adenomyosarcoma"	1
Total	351

of the cervix. They emphasize again the points which are already well known, that cancer of the cervix occurs in married women but fails to appear with expected frequency among Jewish women in spite of their varied social and national backgrounds and their frequently high birth rate.

THERAPY

We come now to the main part of this paper, a consideration of the results of different types of external roentgen therapy on the cure rate. In a search of the literature few studies were found in which any such comparison has been made. Schmitz, Schmitz and Sheehan[10] have compared the results they obtained with radium (3,000–4,000 mg-hr.) and 140 kv. roentgen rays (20.8 per cent gross three year cure rate) with a group treated with radium (4,500 mg-hr.) and 200 kv. roentgen rays (29.2 per cent gross three year cure rate) and with a group of 34 treated with 800 kv. roentgen rays (50 per cent gross three year cure rate). A later report by Schmitz and Sheehan[11] records 26 cases treated with 800 kv. roentgen rays and radium with 12 survivors at five years, or 46.1 per cent.

Several authors have published statistics on the improvement in five year cure rates in cancer of the cervix when roentgen therapy was added to the radium treatment previously used. For instance, Smith and Pemberton[12] report a 42 per cent five year cure rate for patients treated with roentgen rays and radium from 1929 to 1933 inclusive, and compare this with 28 per cent cured between 1924 and 1928 by radium or surgery or both. Of 106 cases treated in 1929 to 1933 with radium alone, 30, or 28 per cent, survived at five years, while of 154 cases treated with radium and roentgen radiation in the same years, 65 survived (42 per cent). That this represents a real increase in survival rate is suggested by their gross survival rate of 38 per cent of all cases seen in these later years.

Meigs and Jaffe[8] report a group of 70 cases with 24 showing clinical cure at the end of five years, or 34.4 per cent. This they attribute to external roentgen therapy.

Several papers have appeared in which varying techniques of radium application have been compared, notably papers by Pitts and Waterman,[9] and the League of Nations reports, so ably reviewed and summarized by Swanberg,[13] but with this question we are not concerned in this paper.

With our own cases we have selected for comparison only those cases in which the following criteria were fulfilled:

1. The diagnosis was confirmed by biopsy.
2. The patient was treated with a vaginal applicator for at least 1,000 mc-hr.
3. A tandem of radon capsules was inserted into the cervix.

TABLE III

FIVE YEAR CURE RATES

387 cases seen from 1932 to 1935 inclusive, proved by biopsy, treated by radium and full roentgen therapy and followed after treatment

	League of Nations Classification											
	Total	Per Cent	Stage I	Per Cent	Stage II	Per Cent	Stage III	Per Cent	Stage IV	Per Cent	Undiagnosed	Per Cent
Massive Dose												
Total	288	100	49	17	98	34	126	44	6	2	9	3
Lost under 5 years	18	6.2	3	6.1	8	8.2	5	4	1	16.7	1	11.1
Dead under 5 years cause unknown or cancer	170	59.0	17	34.7	51	52.0	91	72.2	5	83.3	6	66.7
Dead under 5 years without cancer	8	2.8	1	2.0	3	3.0	4	3.2	0	0	0	0
Alive at 5 years without cancer	82	28.5	26	53.2	32	32.7	22	17.4	0	0	2	22.2
Alive at 5 years with cancer	10	3.5	2	4.0	4	4.1	4	3.2	0	0	0	0
Divided Dose												
Total	99	100	12	12	32	32	48	48	0	0	7	7
Lost under 5 years	6	6.1	1	8.3	3	9.4	1	2.1	0	0	1	14.3
Dead under 5 years cause unknown or cancer	51	51.5	3	25.0	12	37.5	33	68.7	0	0	3	42.8
Dead under 5 years without cancer	3	3.0	1	8.3	1	3.1	1	2.1	0	0	0	0
Alive at 5 years without cancer	35	35.4	6	50.0	16	50.0	11	22.9	0	0	3	42.8
Alive at 5 years with cancer	4	4.0	9	8.3	0	0	2	4.2	0	0	0	0

4. Either "massive dose," "divided dose," or "pyramidal dose" technique of roentgen therapy was used. If less than three-quarters of the scheduled treatment was actually delivered, the case was not considered suitable.

5. The case was followed for at least a month after completion of therapy.

When these criteria are applied, of 597 cases seen and treated between 1932 and 1935 inclusive, 288 are suitable as examples of "massive dose technique" and 99 as examples of "divided dose technique." If the 920 cases seen from 1932 to 1937 inclusive are studied and three year cure rates used, 363 are suitable as examples of "massive dose technique," 163 as examples of "divided dose technique," and 43 as examples of "pyramidal dose technique," or a total of 569. The remaining 351 were considered unsuitable for this study for the reasons listed in Table II.

In Table III are given the five year cure rates of the suitable "divided dose" and "massive dose" cases. They are respec-

TABLE IV

THREE YEAR CURE RATES

569 cases seen from 1932 to 1937 inclusive. These cases include all proved by biopsy, treated by vaginal and cervical radium application, and by full roentgen therapy and followed for at least a month after the completion of the treatment

	League of Nations Classification											
	Total	Per Cent	Stage I	Per Cent	Stage II	Per Cent	Stage III	Per Cent	Stage IV	Per Cent	Unclassified	Per Cent
Massive Dose												
Total	363	100	68	18.7	122	33.6	156	43.0	8	2.2	9	2.5
Lost under 3 years	19	5.2	4	5.9	9	7.4	4	2.6	1	12.5	1	11.1
Dead under 3 years cause unknown or cancer	197	54.3	18	26.5	59	48.3	108	69.3	7	87.5	5	55.5
Dead under 3 years without cancer	9	2.5	3	4.4	3	2.5	3	1.9	0	0	0	0
Alive at 3 years without cancer	123	33.9	40	58.9	45	36.9	35	22.4	0	0	3	33.4
Alive at 3 years with cancer	15	4.1	3	4.4	6	4.9	6	3.8	0	0	0	0
Divided Dose												
Total	163	100	18	11.0	52	31.9	81	49.7	0	0	12	7.4
Lost under 3 years	7	4.3	1	5.5	4	7.7	1	1.2	0	0	1	8.4
Dead under 3 years cause unknown or cancer	86	52.7	5	27.8	21	40.4	54	66.7	0	0	6	50.0
Dead under 3 years without cancer	4	2.5	0	0	2	3.8	2	2.5	0	0	0	0
Alive at 3 years without cancer	59	36.1	12	66.7	22	42.3	20	24.7	0	0	5	41.6
Alive at 3 years with cancer	7	4.3	0	0	3	5.8	4	4.9	0	0	0	0
Pyramidal Dose												
Total	43	100	5	11.6	13	30.2	23	53.5	2	4	0	0
Lost under 3 years	1	2.3	0	0	0	0	1	4.4	0	0	0	0
Dead under 3 years cause unknown or cancer	25	58.2	2	40	7	53.8	14	60.9	2	100	0	0
Dead under 3 years without cancer	1	2.3	0	0	1	7.7	0	0	0	0	0	0
Alive at 3 years without cancer	13	30.2	3	60	4	30.8	6	26.1	0	0	0	0
Alive at 3 years with cancer	3	7.0	0	0	1	7.7	2	8.7	0	0	0	0

tively 35.4 per cent and 28.5 per cent.

In Table IV are the three year cure rates for all suitable "divided dose," "massive dose," and "pyramidal dose" cases. They are 36.1 per cent, 33.9 per cent and 30.2 per cent respectively. The three year survival rates are 40.4 per cent for "divided dosage," 38 per cent for "massive dosage," and 37.2 per cent for "pyramidal dosage."

The increase in five year cure rates from 28.5 per cent to 35.4 per cent by changing the method of external roentgen therapy from "massive dose technique" to "divided dose technique" is impressive. Are these differences in end-results real or are they the result of selection of cases? Obviously, if all the favorable cases were treated by "divided dose technique," one would expect a higher cure rate in this group.

In order to answer this question, the entire group was reviewed by one of us, each history being read with great care, and the case assigned to a League of Nations classification irrespective of how it had been originally classified. In this work the diagrams published in "An Atlas Illustrating the Division of Cancer of the Uterine Cervix into Four Stages"[3] published by the League of Nations, were constantly referred to. It is unfortunate that the League of Nations Committee in 1937 changed the basis of its classification, notably by putting cases formerly classified as Stage IV because of fixation into Stage III, reserving for the former group only cases with extension into the bladder or rectum or distant metastases. Because of this change in classification and because of the confusion arising in some minds between the League of Nations system and that proposed by Schmitz, grouping of cases by classes is often not uniform, and it seemed wiser to attempt a reclassification of all our cases by one man on the basis of the clinical description on the history. While admitting the difficulty in deciding on classification by description alone without recourse to examination, nevertheless, when such a classification is done without reference to the type of treatment the patient subsequently received, any errors should be equal in different treatment groups. Such a classification ought to form a fair basis of comparison of one treatment group with another.

The classification of the three suitable groups according to extent of disease is recorded in Tables III and IV. An inspection of these tables shows that of the "massive dose" cases in the five year group, 17 per cent were in Stage I, 34 per cent in Stage II, 44 per cent in Stage III and 2 per cent in Stage IV, with 3 per cent not classifiable. Of the "divided dose" cases, 12 per cent were in Stage I, 32 per cent in Stage II, 43 per cent in Stage III, and none in Stage IV; 7 per cent were not classifiable. Thus 5 per cent more of the "massive dose" cases fell into the early or operable group than did the "divided dose" cases. Similarly, when we examine Table IV covering all suitable cases from 1932 to 1937 inclusive, we find 18.7 per cent of the "massive dose" cases in Stage I, 33.6 per cent in Stage II, 43 per cent in Stage III, and 2.2 per cent in Stage IV, and 2.5 per cent unclassified. Of the "divided dose" cases, 11.0 per cent are in Stage I, 31.9 per cent in Stage II, 49.7 per cent in Stage III, none in Stage IV, and 7.4 per cent unclassified. Of the "pyramidal dose" cases, 11.6 per cent are in Stage I, 30.2 per cent in Stage II, 53.5 per cent in Stage III, and 4.7 per cent in Stage IV.

Of all suitable cases, 15.9 per cent are in Stage I, 32.9 per cent in Stage II, 45.7 per cent in Stage III, and 1.8 per cent in Stage IV. If we correct by these figures our cure rate for each treatment group, we find the corrected five year cure rate to be 28.1 per cent for the "massive dose technique," and 36.8 per cent for the "divided dose technique," while the three year cure rate is 33 per cent for the cases treated by "massive dose technique," 37.2 per cent for the "divided dose" cases, and 31.6 per cent for the "pyramidal dose" cases. Thus the observed differences in cure rates for various forms of roentgen therapy are *not* dependent on selection of cases by extent of disease. Rather were the less

TABLE V

BIOPSY CLASSIFICATION—MASSIVE DOSE

	Squamous Carcinoma						Adeno-carcinoma		Adeno-canthoma		Not Graded	
	Grade 1	Per Cent	Grade 2	Per Cent	Grade 3	Per Cent	No.	Per Cent	No.	Per Cent	No.	Per Cent
Total	16	6	222	77	30	10	4	1	3	1	12	4
Lost	2	12.5	15	6.8	1	3.5	0	0	0	0	0	0
Died with cancer or?	6	37.5	135	60.8	21	70.0	1	25	1	33.3	5	41.7
Died without cancer	0	0	5	2.3	1	3.3	1	25	1	33.3	0	0
Living at 5 yr. without disease	8	50.0	62	27.9	6	20.0	2	50	1	33.3	5	50
Living at 5 yr. with disease	0	0	5	2.3	1	3.3	0	0	0	0	1	8.3

BIOPSY CLASSIFICATION—DIVIDED DOSE

	Squamous Carcinoma						Adeno-carcinoma		Adeno-canthoma		Not Graded	
	Grade 1	Per Cent	Grade 2	Per Cent	Grade 3	Per Cent	No.	Per Cent	No.	Per Cent	No.	Per Cent
Total	3	3	80	80	9	9	3	3	2	2	2	2
Lost	1	33.3	5	6.3	0	0	0	0	0	0	0	0
Died with cancer or?	1	33.3	41	51.0	4	44.5	2	66.6	2	100	1	50
Died without cancer	0	0	3	3.8	0	0	0	0	0	0	0	0
Living at 5 yr. without disease	1	33.3	28	35	5	55.5	1	33.3	0	0	1	50
Living at 5 yr. with disease	0	0	3	3.8	0	0	0	0	0	0	0	0

favorable cases treated by the more successful "divided dose" type of therapy.

Can the apparent superiority of the "divided dose technique" be explained on the basis of the age distribution of the patients in the treatment groups? In general, the older patients were treated by "massive dose," since this entailed fewer visits to the hospital and less physical effort. For instance, between 1932 and 1935, 47 per cent of the patients receiving "massive dose" therapy were under fifty and 53 per cent were fifty or over, while 65 per cent of the patients receiving "divided dose" therapy were under fifty and 35 per cent over fifty. How little significance this has is seen when it is pointed out that of all suitable cases treated over five years ago those over fifty showed a higher five year survival rate, 36 per cent, than did those under fifty, 32 per cent. That is, the older patients treated by "massive dose technique" really constituted the more favorable cases. In spite of this they did not do so well as the younger patients receiving "divided dose technique." If we correct for age distribution in the two groups, we find a 31.9 per cent five year cure rate for "massive dose"

therapy and a 39.4 per cent cure rate for "divided dose" therapy.

Finally, is it possible that the difference in cure rate for massive and divided dose therapy can be explained on the basis of histopathological classification of cases? Is it possible that the more slowly growing and perhaps more favorable histopathological types of tumors were treated more by one technique than the other, therefore give a better cure rate for that technique? In Table v is seen the classification of the 386 suitable cases by biopsy report. It is noted that in the group treated by "massive dose technique" 6 per cent were in Grade 1 with a 50 per cent cure rate, 77 per cent in Grade 2 with a 27.9 per cent cure rate, and 10 per cent in Grade 3 with a 20 per cent cure rate. In the "divided dose" group, 3 per cent were in Grade 1 with 33 per cent cures, 80 per cent in Grade 2 with 35 per cent cures, and 9 per cent in Grade 3 with 55.5 per cent cures. If this inequality of histopathological picture be corrected for again the difference in five year cure rate between the two groups is made more rather than less marked, 29.5 per cent for "massive dose" and 37.7 per cent for "divided dose."

In brief, then, in our clinic comparable groups of cases treated exactly the same except for the type of external roentgen therapy received show that the so-called "divided dose technique" gave a 35.4 per cent five year cure rate, while "massive dose technique" gave 28.5 per cent. These differences are made more marked rather than less if the statistics are corrected for extent of disease in the two groups, age distribution, or histopathological classification. That the difference in cure rates is real is further suggested by larger numbers of cases followed only three years in which again a decided increase in cure rate is seen in those receiving the "divided dose" therapy.

SUMMARY

1. Nine hundred and twenty cases of primary carcinoma of the cervix observed in Memorial Hospital from 1932 to 1937 inclusive are reported and reviewed.

2. The peak in age incidence in this group lay between forty and fifty-five.

3. Only 24 of the 920 cases were single and of these 6 admitted that they had borne children.

4. Of foreign born patients, Italians showed the highest incidence of cervical cancer.

5. Negroes formed 8.5 per cent of the group.

6. Only 46, or 5 per cent, of the cases were Jewish, in spite of the large number of Jews in the population of New York City.

7. When the same kind and amount of radium was given to patients treated by different types of external roentgen therapy, it was found that a 28.5 per cent five year cure rate followed the so-called "massive dose technique," while 35.4 per cent followed the "divided dose technique." This difference was not due, as far as could be determined, to the extent of the disease in the patients making up the two groups, the age of the patients, or the histopathological grades of tumor found to be present.

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THE PRODUCTION AND CHARACTERISTICS OF 3,000 KILOVOLT ROENTGEN RAYS*

By J. G. TRUMP, D.Sc., *and* R. W. CLOUD, M.A.
Massachusetts Institute of Technology
CAMBRIDGE, MASSACHUSETTS

FOLLOWING the development and installation for medical use of a 1,000 kv. air-insulated electrostatic roentgen-ray generator at the Huntington Memorial Hospital in Boston in 1937[1] and of a 1,250 kv. compressed air-insulated generator at the Massachusetts General Hospital[5] in 1940, the High Voltage Group of the Massachusetts Institute of Technology undertook the extension of the electrostatic method to substantially higher voltages.

The resultant generator has produced roentgen rays at steady, constant voltages up to 4,000 kv., using air at 13 atmospheres pressure as the insulating medium, and has produced radiation at voltages up to 4,700 kv., using a combination of air and Freon (CCl_2F_2) at this pressure. For the past year this generator has been used to study the physical properties of roentgen rays produced at these elevated voltages, and particularly to observe the progressive change in these properties over the entire voltage range. Since the spring of 1942, the generator has been available for radiation therapy at 3,000 kv., the preliminary results of which are to be presented by Dr. Richard Dresser in a companion paper.

HIGH VOLTAGE SOURCE

It may be well to review briefly the operating principles of the Van de Graaff type of electrostatic high voltage source and the general features of the generator and tube used in this work. The voltage source, as shown in Figure 1, consists essentially of a well rounded, high voltage terminal about 2 ft. in diameter supported from the ground by a column structure of alternate insulating and metallic spacers. A single insulating belt 12 in. wide travels at high speed within the column and transfers electric charge continuously between ground and terminal. The terminal voltage

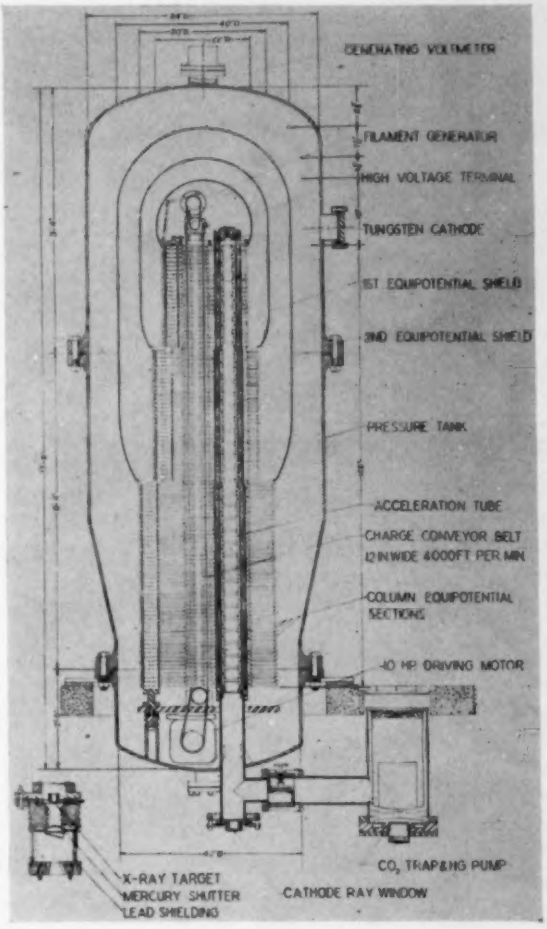

FIG. 1. Roentgen-ray and cathode-ray generator.

of the generator is evenly divided lengthwise of the column by means of resistors so as to produce a uniform gradation in potential from the terminal to the ground plane. This assembly is mounted within a metal

* Presented at the Forty-third Annual Meeting, American Roentgen Ray Society, Chicago, Ill., Sept. 15–18, 1942.

pressure tank so that by compression of the gas the electrically charged belt, terminal, and column may be insulated with a medium superior to air at ordinary pressures. The inside dimensions of this tank are 4½ ft. diameter by 13 ft. high.

In operation, negative electric charge is sprayed on the insulating belt at its lower end and hauled up into the high voltage terminal, which acquires a negative potential relative to ground in direct proportion to the stored electric charge. The generator will operate at that equilibrium voltage at which the current transferred to the terminal by the belt is just equal to the current through the roentgen tube and the leakage and control currents characteristic of operation at that voltage. This equilibrium voltage value may be adjusted from a few hundred thousand volts to the maximum voltage by controlling the current sprayed on the charge-conveyor belt.

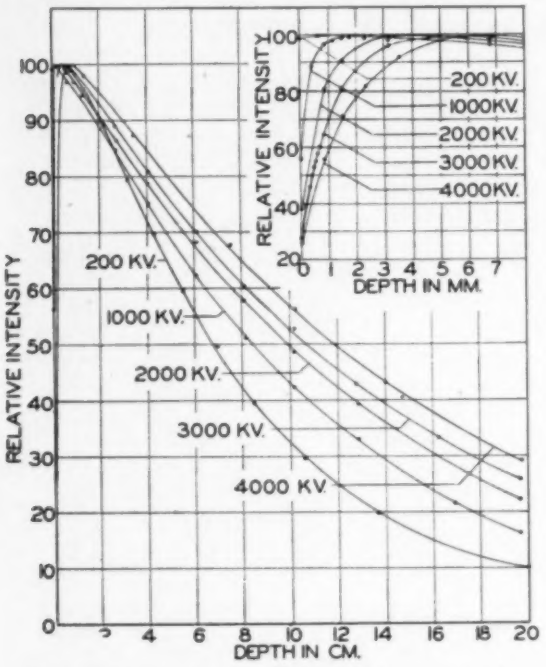

Fig. 2. Depth dose in masonite phantom with 10 by 10 cm. field at 70 cm. distance.

Kilovoltage	Filtration	
200		0.5 mm. Cu
1000	2 mm. Pb	5 mm. Cu
2000	6 mm. Pb	5 mm. Cu
3000	10 mm. Pb	5 mm. Cu
4000	20 mm. Pb	5 mm. Cu

Roentgen Tube

The continuously pumped roentgen tube is located axially within the generator column, the insulating portion extending from a point within the high voltage terminal to the ground end of the column. Beyond this, a metal extension of the tube passes out through the tank bottom and terminates in a water-cooled gold target surrounded by a suitable thickness of lead shielding and provided with beam-defining portals and shutter. The roentgen tube is built up of 100 glass rings between each of which is placed a metallic accelerating and focusing electrode connected to the generator column at that level. The electrons originating at the tungsten filament at the high voltage terminal end of the tube are thus progressively accelerated and focused as they pass axially downward until they arrive at the target with full terminal energy in a well defined focal spot about 1 cm. in diameter.

"Subcutaneous Effect"

The distribution in material of unit density of the ionization produced by roentgen rays over the voltage range of 1,000 to 4,000 kv. has been investigated with this apparatus. Perhaps the most outstanding characteristic at these voltages is the progressive movement of the region of maximum ionization to a depth farther below the surface as the voltage is increased. This phenomenon, which is hereinafter termed "subcutaneous effect," is hardly apparent at 200 kv. As shown in the insert of Figure 2, the ionization intensity for 200 kv. radiation remains practically constant for the first 5 mm. below the surface.

For 1,000 kv. radiation, the "subcutaneous effect" is already considerable and is sufficient to account, in part at least, for the decreased skin erythema which has been demonstrated in this voltage region.[2] The surface ionization intensity at 1,000

kv. begins at about 60 per cent of the maximum value and rises with decreasing rapidity to the maximum found nearly 2 mm. below the surface. Beyond this depth, the intensity falls off slowly in accordance with the laws of absorption and the inverse square law.

For increasing voltages, the depth below the surface at which the ionization intensity has increased to 95 per cent of its maximum value is 0 for 200 kv. radiation, 0.8 mm. for 1,000 kv., 2 mm. for 2,000 kv., 3 mm. for 3,000 kv., and 4 mm. for 4,000 kv. At the same time, the surface intensity diminishes from 98 per cent of the maximum value for 200 kv. radiation, to 56 per cent for 1,000 kv., 38 per cent for 2,000 kv., 28 per cent for 3,000 kv., and 26 per cent for 4,000 kv.

This "subcutaneous effect," observed only for radiation of considerable energy, is due primarily to the increase in the number of secondary electrons in the beam as it penetrates and traverses the phantom material. The depth at which the number of electrons in the beam stops increasing, i.e., the depth of maximum ionization, depends on the average range of the electrons in the phantom material. Since an increased tube voltage increases the range of secondary electrons, it will also increase to a corresponding extent the depth at which maximum ionization occurs. The range of secondary electrons, negligible at 200 kv., becomes sufficient at 1,000 kv. to move the depth of maximum ionization several millimeters below the surface. This tendency increases with voltage. The influence of secondary roentgen rays, on the other hand, is predominant at 200 kv. and diminishes with increasing voltage. Beyond 2,000 kv. the effect of secondary roentgen rays on the distribution of ionization in the material is relatively negligible.

DEPTH DOSE

Figure 2 shows the depth dose over a range of voltages at a distance of 70 cm. with a 10 by 10 cm. field. It is to be noted that the filtration is increased from the standard value of 0.5 mm. copper for 200 kv. to the value of 20 mm. lead and 5 mm. copper at 4,000 kv. Observing the relative intensity at a depth of 10 cm., a steady increase with voltage from 32 per cent at 200 kv. to 57 per cent at 4,000 kv. is noted. The influence on "subcutaneous effect" and

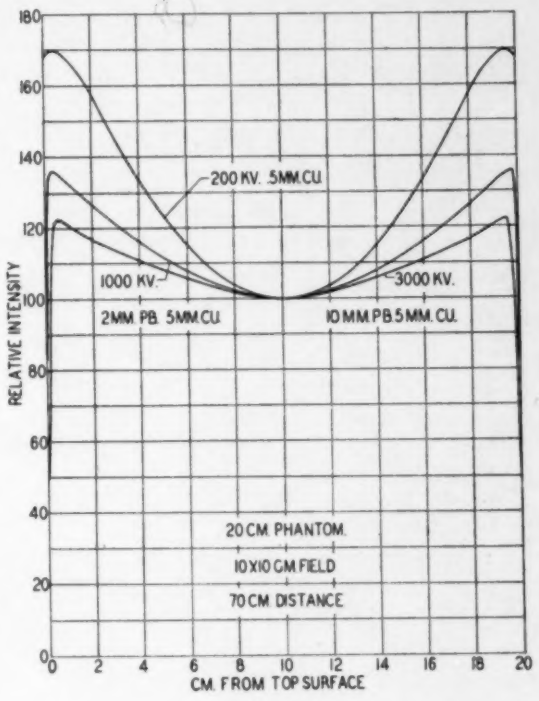

Fig. 3

on depth dose has been studied as a function of treatment distance, filtration, and field size. These measurements show little change in "subcutaneous effect" with increase of 70 to 100 cm. distance, but the depth dose is increased almost as would be expected from the inverse square law. Addition of filtration increases the 10 cm. depth dose and accentuates the "subcutaneous effect," the first increments of filtration being relatively more effective. At 3,000 kv., the 10 cm. depth dose with the 10 by 10 cm. field is 52 per cent at 70 cm. and 57 per cent at 100 cm. The half-value layer in lead for 3,000 kv. roentgen rays filtered with 10 mm. lead and 5 mm. copper is 9.8 mm. Scattering remains small in the 1,000 to 4,000 kv. range, the scattering at

higher voltages being due almost entirely to secondary electrons.[4]

Figure 3 shows the distribution of ionization in a 20 cm. phantom irradiated from two opposite portals with 200, 1,000, and 3,000 kv. roentgen rays. The intensity measurements have been adjusted to 100 per cent at the center of the phantom (10 cm. depth) so that the curves show the relative intensities both at the skin and at the region of maximum ionization for the same intensity at the depth. It is seen that at 200 kv. approximately 170 per cent of the 10 cm. dosage will be delivered to the skin and first 5 mm. At 1,000 kv. the intensity at the skin is about 90 per cent of the 10 cm. value and increases to 135 per cent at 2 mm. For 3,000 kv. the intensity at the skin begins at 50 per cent of the 10 cm. value and increases to 123 per cent at a point 5 mm. below the surface of the skin. This illustration shows, for the simple case of two opposite portals, that the higher voltage roentgen rays will produce a substantially lower dose at the skin and in the intervening region for a given intensity at the depth.

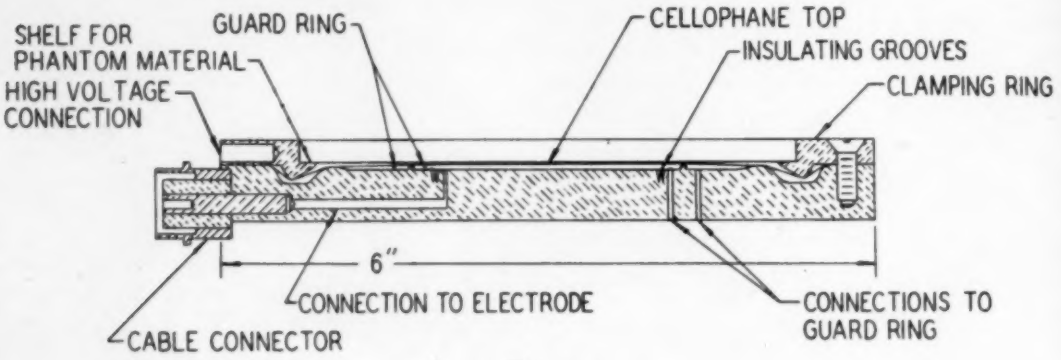

Fig. 4

Method of Measurement

It is evident that precise determinations of the distribution of ionization in depth must be performed with an ionization chamber of negligible thickness.[3] Figure 4 shows the ionization chamber with which this distribution was determined. The bottom of the chamber is made of lucite, an insulating plastic of density 1.2, which is considered as part of the phantom. The upper electrode consists of a sheet of stretched 0.02 mm. cellophane with a conducting coating. By this means, a thin air chamber with an active space $2\frac{1}{16}$ in. in diameter and 1 mm. thick surrounded by a guard ring is obtained. The ionization chamber is submerged in a 30 cm. cube phantom composed of masonite hardboard, and the effect of moving the chamber below the surface is obtained by placing thin layers of corresponding material over the upper surface. A second control chamber is placed 20 cm. from the target to compensate for changes in tube current during readings.

A study was made of the relative merits of a thin-disk ionization chamber and a standard Victoreen thimble chamber in the measurement of extremely penetrating roentgen rays. This indicated that, while the Victoreen thimble chamber is not useful for determining the distribution of ionization close to the surface, it can under proper conditions be used for the determination of the maximum ionization or of the intensity at any substantial depth. When a Victoreen thimble chamber is laid on the surface of the phantom, it will read an intermediate value unless covered with a sufficient thickness of air-wall material to bring the secondary ionization to an equilibrium condition. For 3,000 kv., 3 mm. of lucite or

similar material is an adequate thickness.

In supervoltage roentgen therapy, it is desirable that the subcutaneous dose of maximum intensity be taken as the measure of the incident dose.*

The authors take pleasure in acknowledging the generous grant of the Godfrey M. Hyams Trust which has made possible this and previous work at the Massachusetts Institute of Technology on supervoltage techniques. The able assistance of Floyd McIntosh and John C. Stacey is also gratefully acknowledged.

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* For discussion see page 537.

PRELIMINARY CLINICAL OBSERVATIONS ON THE USE OF 3 MILLION VOLT ROENTGEN RAYS*

By RICHARD DRESSER, M.D.
BOSTON, MASSACHUSETTS

IN 1936 a new method for the production of supervoltage roentgen rays was presented at the annual meeting of the American Roentgen Ray Society.[1] An electrostatic generator capable of producing somewhat over a million volts was described. This machine was used for cancer treatment and research at the Collis P. Huntington Memorial Hospital, Boston. The original apparatus was dependent on air insulation, and a considerable space was required for its housing. A second more compact million volt unit operating on the electrostatic principle but insulated by air under pressure has been installed at the Massachusetts General Hospital.[5] A third pressure insulated unit which has been operated at 3 million volts for therapeutic purposes is now in use at the Massachusetts Institute of Technology.

Roentgen rays produced at 3 megavolts have essentially the same physical properties as the gamma rays of radium. However, the high roentgen intensity permits long treatment distances with the result that the depth dose is much greater than it has been possible to obtain with teleradium therapy. It is nearly double the 200 kv., 10 cm. depth dose. In view of this high intensity and increase in depth dose, it has been deemed advisable to proceed with caution in the therapeutic application of these rays. Only cases of pelvic cancer have thus far been irradiated since the factors of absorption, scattering, etc., in this part of the anatomy are analogous to those measured in a phantom. The patients have been treated in groups, with allowance of a sufficient time interval between groups for the observation of any untoward symptoms. All patients received successive daily exposures of 400 r each, delivered to the anterior pelvis through either 15 by 15 cm. or 10 by 10 cm. portals of entry. The larger portal was employed in most instances.

Ionization measurements show that the intensity measured directly on the surface is somewhat less than the intensity measured 4.5 to 5 mm. below the surface. Roentgen dosage is therefore calculated not from the surface measurement, but from the subcutaneous point of greatest ionization. The portal of entry is delineated by means of a light beam, and the coning mechanism is placed well above the patient. The clothes are always removed from the surface irradiated. The treatment factors employed are as follows: 3 million volts constant potential, 100 cm. distance, 10 mm. lead plus 5 mm. copper filter. At 0.5 milliampere the subcutaneous roentgen intensity averages 90 r per minute with the portals employed.

The first group of patients received a total of 1,200 r, that is, three daily treatments of 400 r each. During the follow up period of a month there was no visible skin reaction, and no symptoms of irritation of the bladder or intestine developed. The second group received five daily exposures totaling 2,000 r. During the observation period there was no superficial reaction and no intestinal disturbance. The third group was given 2,400 r which caused diarrhea in all cases but there was no erythema or epilation. The fourth group received 2,800 r which is the largest dose thus far administered. These patients experienced rather severe diarrhea together with some bladder irritation. In no instance, however, was there any redness of the skin or falling out of the pubic hair. All patients tolerated the treatment remarkably well with one exception. This was a case of extensive carcinoma of the bladder, and it was subsequently observed that the response to 200 kv. radia-

* Presented at the Forty-third Annual Meeting, American Roentgen Ray Society, Chicago, Ill., Sept. 15–18, 1942.

tion was no better than to supervoltage therapy.

These preliminary clinical findings substantiate the observation that as the wave length of a roentgen-ray beam is decreased the skin tolerance and depth dose are increased.[2,3,4] Because of reaction in the deeper structures a total of 2,800 r to a single pelvic portal has not been exceeded. This is apparently a suberythema dose. It is anticipated that larger amounts of radiation will be tolerated in other parts of the body where the underlying structures are less vulnerable than the intestine and bladder.

No attempt has yet been made to evaluate the effect of 3 million volt roentgen rays on new-growths. The number of patients irradiated thus far has been small, and the maximum follow up period at the time of writing is only five months. The largest tumor dose has been somewhat less than we are accustomed to deliver with 200 kv. roentgen rays. However, the supervoltage dose has been administered in a period of a week, whereas our usual 200 kv. pelvic series extends over a period of about three weeks. The immediate reaction in the deep tissues resulting from supervoltage radiation has been fully as severe as that observed following treatment at lower potentials. The acute symptoms of intestinal and bladder irritation are of approximately the same duration. Thus far there have been no untoward late sequelae.

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DISCUSSION ON PAPERS BY DRS. TRUMP AND CLOUD, AND DRESSER

Dr. K. E. Corrigan, Detroit, Mich. I find myself overawed by the accomplishment of Professors Trump and Cloud in building such a relatively small and compact machine to develop so much power, and to operate in such an apparently reliable and routine manner. It would be difficult to say too much in praise of their engineering ability and technical skill.

The measurements they have presented on the output of this tube are also a real contribution, particularly the measurement of the depth of maximum effect.

It would have been interesting to hear something about the output intensity of this tube. Of course this brings up the old discussion on the use of thimble chambers at this voltage, but perhaps Dr. Dresser will give us some idea of the r per minute per microampere.

Another point I would like to have Dr. Dresser discuss arises from the measurements on both sides of the 20 by 20 cm. phantom. In actual application the beam passes through the patient's body and is at equilibrium with its secondaries on the exit side. In addition the exit portal gets whatever secondary may arise from the material on which the patient is lying. Consequently the exit dose is really a depth dose, and is quite a different thing from a dose of primary radiation applied to the surface from outside.

The authors have made the best possible use of their time, and told us as many of the important points as possible. We can only wait patiently for them to have an opportunity to give us some absorption curves and other important data.

Professor Trump and his associates are to be congratulated for an outstanding advance in physics and technology and for a very fine paper.

Dr. T. Leucutia, Detroit, Mich. These reports dealing with the physical and clinical aspects of a new apparatus for the treatment of cancer represent further most valuable contributions to our radiologic practice. Ever since the advent of supervoltage roentgen therapy, Drs. Trump and Dresser have pursued with great zeal the production of such rays by the old-fashioned electrostatic generator which they have streamlined. After repeatedly traversing unexplored ranges, they now have reached the formidable domain of 4.7 megavolts. The physical achievements are impressive. A yield of 90 r per minute, for example, with a 10 mm. lead and a 5 mm. copper filter at 100 cm. distance with only 0.5 ma. current at 3 megavolts, or a depth dose of nearly double that obtained with 200 kv., are accomplishments that cannot remain without influence in our present-day roentgen therapeutic conception.

The clinical observations, as Dr. Dresser stated, are as yet in the preliminary stage, but even so, it is gratifying to see factual confirmation up to 3 megavolts of the so often disputed theoretical conjecture that with increasing voltages there is an increased tolerance of the skin. On the other hand, a total of 2,800 r, in daily fractions of 400 r, administered over a single pelvic portal, without even producing an erythema, but leading to marked diarrhea with some bladder irritation, is a new type of dose which merits our earnest consideration. Such a dose may do away with the present complicated methods of cross-firing of the deep roentgen therapy, a fact which is responsible for the ever accumulating series of permanent injuries to the normal structures. It is therefore to be hoped that the authors will continue their investigations in the future with equal zeal and that soon they will be able to make additional reports on this most interesting subject.

Dr. Donald W. Kerst, Urbana, Ill. Are there many secondary electrons produced by the cone of the roentgen-ray equipment? In order to obtain the rise in ionization under the skin is it necessary to remove these secondary electrons which would bombard the skin?

Dr. Dresser (closing). First, I should like to thank Dr. Leucutia for his encouraging discussion of the joint paper, and then I shall try to answer the questions that Dr. Corrigan has put.

The first one I think has already been answered in regard to the output of the tube. At 0.5 ma. at a distance of 100 cm., with 10 mm. of lead and 5 mm. of copper ground filter, the output runs 80 to 90 roentgens per minute.

Now as to the exit dose, unfortunately I cannot give any accurate data. This has not been studied in any particular detail. From the charts that Professor Trump and his co-workers have compiled, the exit dose from a field 10 by 10 cm. should be approximately 25 per cent of the maximum subcutaneous dose, but further than that I cannot go.

Then there was a question as to the use of the Victoreen chamber. Apparently the chamber gives relatively accurate air and surface measurements if it is surrounded with a small lucite thimble. Professor Trump and his collaborators have made such a thimble, which is about 3 mm. thick for 3 megavolt rays, and simply slips on over the standard chamber. Then the measurement of air and surface intensities becomes analogous to that made on low voltage radiation with the standard thin wall chamber. In measuring doses below the surface of a phantom it is not necessary to alter the Victoreen chamber in any way. The measurements are perfectly accurate.

In regard to the removal of secondary electrons, let me stress the point that the coning of the beam is done well above the patient, 50 cm., and also care is taken to remove the clothes so that the maximum intensity is delivered as far below the surface as possible. If material of low density is placed on the patient's skin and built up to a thickness of say 5 mm. then the point of maximum ionization occurs directly on the skin.

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THE AMERICAN JOURNAL OF ROENTGENOLOGY AND RADIUM THERAPY

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Forty-fourth Annual Meeting: 1943, cancelled.

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Twenty-eighth Annual Meeting: 1943, cancelled.

EDITORIALS

MEGAVOLTAGE ROENTGEN THERAPY

IT IS customary to designate as supervoltage roentgen therapy that form of irradiation which is carried out with roentgen rays produced by voltages above 250 kv. When the term was originally introduced, the aim was to create a segregation from deep roentgen therapy, and for obvious reasons no attempt was made to limit the upper range to which such therapy may be extended. Recently, important contributions by Trump and Cloud,[1] by Dresser[2] and by Koch, Kerst and Morrison[3] with roentgen rays up to 20 million volts have brought to light certain new features of the physical dose and biological effect which suggest that perhaps the time has now arrived to try to establish where the upper line of demarcation may be drawn and whether or not further segregation may appear advisable from the practical standpoint.

The studies of Trump and Cloud[1] and of Dresser[2] were carried out with roentgen rays produced by voltages from 1 million to 4 million volts constant potential. The most outstanding observation made by these authors was the fact that the ionization in the layers underneath the skin was larger than on the surface of the skin and that the region of maximum ionization moved progressively below the surface as the voltage was increased. This effect, which the authors called the "subcutaneous effect" led to the unusual clinical experience that in patients afflicted with cancer of the cervix such large depth doses could be administered through one single anterior pelvic field that rather severe diarrhea and some bladder irritation resulted without there being any redness of the skin or even epilation of the pubic hair. Obviously a new type of dosage was encountered.

The investigations of Koch, Kerst and Morrison[3] were extended to the range of 20 million volts. To Kerst[4] falls the merit of having made possible the generation of roentgen rays at such extremely high voltages. He, with the ingenuity of a true scientist, solved the not altogether new idea of circular acceleration of the electron and after assiduous work he succeeded in building a new type of roentgen apparatus which he called the betatron. This apparatus somewhat resembles a small cyclotron but its operation is entirely different. The electrons, injected from an electron gun into a circular path within a doughnut-shaped high vacuum roentgen tube, are accelerated by an induction scheme which permits the continuous and direct application of the electromotive force to their stream. In consequence, it is possible to reach, with very small equipment, energies in electron volts corresponding to the voltages generated in the secondary windings of huge transformers. The 20 million betatron has 1 inch of pole diameter

[1] Trump, J. G., and Cloud, R. W. The production and characteristics of 3,000 kilovolt roentgen rays. Am. J. Roentgenol. & Rad. Therapy, April, 1943, *49*, 531–535.

[2] Dresser, R. Preliminary clinical observations on the use of 3 million volt roentgen rays. Am. J. Roentgenol. & Rad. Therapy, April, 1943, *49*, 536–538.

[3] Koch, H. W., Kerst, D. W., and Morrison, P. Experimental depth dose for 5, 10, 15 and 20-million-volt x-rays. *Radiology*, February, 1943, *40*, 120–127.

[4] Kerst, D. W. Acceleration of electrons by magnetic induction. *Phys. Rev.*, 1940, *58*, 841.

Kerst, D. W. Acceleration of electrons by magnetic induction. *Phys. Rev.*, 1941, *60*, 47–53.

Kerst, D. W., and Serber, R. Electronic orbits in the induction accelerator. *Phys. Rev.*, 1941, *60*, 53–58.

Kerst, D. W. A twenty million electron-volt betatron or induction accelerator. *Rev. Scient. Instruments*, 1942, *13*, 387–394.

Kerst, D. W. The betatron. *Radiology*, February, 1943, *40*, 115–119.

per 1 million volts but there is now under construction a 100 million volt betatron which will necessitate only ¾ inch of pole diameter per 1 million volts, thus further reducing material and space.

The experimental results obtained by Koch, Kerst and Morrison[3] entirely confirmed the observations made by Trump and Cloud, and Dresser, and they have demonstrated that at ranges up to 20 million volts the ionization below the surface may amount to several times the incident dose and that the region of the maximum ionization may lie several centimeters below the surface. If, for example, at a target distance of 45 cm. the surface dose was taken as 100 per cent, the maximum ionization amounted to 125 per cent for 5,000 kv., 185 per cent for 10,000 kv., 245 per cent for 15,000 kv. and 310 per cent for 20,000 kv., and the regions of maximum ionization were approximately 1, 2, 2.5 and 3 cm. below the surface for the respective voltage ranges. The depth dose at the conventional 10 cm. below the surface amounted to over 70 per cent for 5,000 kv., 120 per cent for 10,000 kv., 170 per cent for 15,000 kv. and nearly 230 per cent for 20,000 kv. Although these authors did not extend their observations to clinical patients, results along the lines noted by Dresser[2] undoubtedly would be obtained.

The explanation of these new phenomena at very high voltages is most interesting. Failla, Twombly and Marinelli[5] first described what they called the electron equilibrium level of a roentgen beam. They have shown that when a roentgen- (or gamma) ray beam strikes the skin of a patient—or the surface of any phantom used for depth dose measurements—it contains a mixture of secondary electrons from filters, cones, etc., as well as from stray collisions with objects near the beam. Furthermore, there is an addition of electrons from the very superficial layers of the absorbing medium (skin or material of the phantom). As a result, an increasingly larger proportion of ionization is found immediately underneath the surface until at a certain level an equilibrium of the electrons consistent with the quality of the beam and the physical characteristics of the medium is reached. Exhaustive measurements demonstrated that this electron equilibrium level lies within fractions of a millimeter from the surface at 200 kv. (peak) radiation and at a depth of about 1.5 mm. at 1,000 kv. (pulsating) radiation. The biological importance of such an effect on the variation of the surface dose, especially as far as the skin erythema is concerned, was stressed in a former editorial in this JOURNAL.[6]

The extension of the electron equilibrium theory to the radiations produced by the very elevated voltage ranges investigated by Trump and Cloud, and Dresser, and by Koch, Kerst and Morrison encounters no difficulty. The main difference is that here the ionization is entirely due to Compton electrons the range of which plays a paramount rôle. At the voltages studied by Failla, Twombly and Marinelli[5] the ionization from the Compton electrons appeared very near the point where the Compton process occurred, exercising no particular effect on the shape of the depth dose curves. Above 1,000 kv., however, the range of the Compton electrons increases progressively and so rapidly that it leads to increase of the depth dose, on the one hand, and movement of the region of the maximum ionization, on the other. According to Koch, Kerst and Morrison[3] the electrons produced in the Compton process of a roentgen-ray beam from a 20 million betatron may have a range as great as 10 cm. in tissue. Since one may assume that constant ionization is produced along the entire tract of such an electron until the end of its range, it becomes clear that the increase with depth in the number of such electrons must result in gradual increase of the ionization above

[5] Failla, G., Twombly, G., and Marinelli, L. D. A method for decreasing the ionization in the skin applicable to supervoltage x-ray therapy. *Radiology*, 1930, *28*, 693–703.

[6] Leucutia, T. The necessity of a coordinated biological dose system in radiation therapy. (Editorial.) AM. J. ROENTGENOL. & RAD. THERAPY, 1941, *46*, 883–887.

that encountered near the surface, leading to a proportionately larger depth dose. The maximum of the ionization is reached at a certain critical level underneath the surface characteristic of the quality of the roentgen-ray beam applied. The gradual absorption of the electrons is followed by a corresponding fall of the ionization and with it of the depth dose.

Evidently, when clinical radiation therapy is administered under such conditions the situation encountered is entirely different from that to which we are accustomed in the ranges below 1,000 kv. Perhaps some advantage may be derived, therefore, by restricting the field of supervoltage roentgen therapy to the limits of from 250 to 1,000 kv. and by creating an entirely new domain for the voltages above 1,000 kv., which then is called megavoltage roentgen therapy. The particular range could be designated by placing the corresponding number of megavolts in a prefix, as, for example, 5, 10, 15 or 20 megavolt therapy.

Exhaustive clinical studies will be required to properly evaluate the therapeutic significance of this extremely penetrating type of radiation and especially its rôle in the simplification of the present day difficult methods of technical application. A great deal could be gained, however, by first trying to establish some correlation between the experimental physical dose as determined by the above investigators and the biological dose as administered to patients. If possible, such correlation may be incorporated into a uniform system of dosimetry including all voltage ranges employed in clinical practice.

It has been suggested formerly in this Journal[6,7] that the biological unit, "skin unit dose," designated with the abbreviation s.u.d., used in conjunction with the r, would have many advantages in specifying a certain dose. This unit has been defined as a surface dose unit and it has been given a physical value, measurable in r, the magnitude of which changes with various voltages. In the ranges used so far it always represented a higher value than the depth dose at any point, except the infinitesimal layers near the surface which are hardly significant from the point of view of clinical application. It has become convenient to express a certain tumor dose in so many per cent of the skin unit dose and since the damage of the skin forms the greatest barrier to any biological overdosage, a measure of safety could easily be established.

In the megavoltage roentgen therapy, the surface dose represents a smaller value than the depth dose. As has already been stated, the ionization progressively rises to a peak which with increasing voltages lies at gradually deeper layers, becomes broader and acquires a proportionately greater value. Furthermore, the surface dose itself can be critically affected by electrons escaping from the original beam of the acceleration chamber of the betatron or by Compton electrons scattered from neighboring objects. Therefore, if the s.u.d. is introduced as a biological unit, this may be employed in two ways. First, as an extension from the lower voltage ranges in the form of a surface dose unit. In this case, its physical magnitude is determined experimentally along the entire megavoltage scale and the depth dose curves are plotted in percentages of the surface dose. If, for example, a dose of 130 per cent s.u.d. (the maximum compatible with safety) is desired at a certain depth, this will represent a percentage of the s.u.d. as measured on the skin. By using such a procedure, even should stray electrons affect the surface dose, the danger of harm is less than if a too large depth dose were administered at a certain level. Of course the region as well as the broadness of the maximum ionization must also be stated. The second alternative is to calculate the dose not from the surface measurement but from the region of greatest ionization, in which case the s.u.d. would in fact represent a tissue (depth) dose unit. This method, in its

[7] Leucutia, T. Physical and biological dosage in radiation therapy. (Editorial.) Am. J. Roentgenol. & Rad. Therapy, 1937, *38*, 367–369.

physical equivalent, i.e., by actually measuring the r, is preferred by Trump and Cloud,[1] and Dresser,[2] as well as by Koch, Kerst and Morrison.[3] The peak ionization is taken as 100 per cent and the doses at the surface as well as at various depths are plotted in fractions of the peak ionization. The region of the peak ionization is stated separately for each location.

It is as yet too early to visualize what form megavoltage roentgen therapy will take in clinical application. The future, however, appears rich in promise and the road leading to it is no longer strewn with insurmountable obstacles.

T. Leucutia

JOSEPH FRANCIS ELWARD
1890–1943

TO MY mind, the saddest words an obituary can contain are "after a long illness." Dr. Joseph F. Elward died on February 6, 1943, in Plains, Pennsylvania, after a very long illness.

Dr. Elward was born in Plains, Pennsylvania, on July 4, 1890. He obtained his early education in Plains and from there he went to the Philadelphia College of Pharmacy from which he was graduated in 1913. Following his graduation he returned to Plains and opened his own drug store. After two years, however, he decided to study medicine and he entered Georgetown Medical School in Washington, D. C., where he attended classes in the daytime and worked

evenings as a registered drug clerk. He was graduated from Georgetown in 1919, president of his senior class, and received an appointment as intern in Providence Hospital in Washington. After serving his internship he opened an office in Washington, engaging in general practice. However, an otitis media dating from childhood made him believe that he had progressive deafness to look forward to, and it seemed wiser to take up a specialty where he would depend less on his hearing and more on his eyesight. He therefore decided to specialize in roentgenology and he served as intern under Dr. P. F. Butler at the Boston City Hospital, Boston, in the Department of Roentgenology from April 1, 1924 to May 1, 1925 and as assistant physician in the Department from May 1, 1925, until August 31, 1925.

Dr. Elward then returned to Washington, D.C., where he became associated with Dr. Charles A. Pfender. Dr. Pfender died in 1926 and Dr. Elward opened his own office for the practice of radiology. In addition to his private practice, in which he was very successful from the beginning, he was Clinical Professor of Roentgenology in Georgetown Medical School and Instructor in Radiology in George Washington Medical School and was radiologist to George Washington and Sibley Hospitals. Notwithstanding this full schedule he found time to devote to research and to the writing of many scientific papers on a variety of subjects.

In 1935 Dr. Elward suffered from a coronary attack and within a year he sustained a second one. With periods of enforced rest he still carried on his practice which always grew larger and he still continued to write many valuable scientific papers. However, late in 1940 he had a cerebral accident which produced at first a slight aphasia and he was never able to work again. He retired to the home of his three sisters in Plains where he remained until the time of his death. To me, his devoted friend for a quarter of a century, it was tragic to witness his gradual transition from a power among men to an invalid progressively feebler in body but indomitable in spirit to the last.

Dr. Elward is survived by his wife, the former Mary Tourville of Plains, two daughters and one son, three sisters, two brothers, and his devoted stepmother.

Dr. Elward was a member of the American Roentgen Ray Society, the Radiological Society of North America, the American College of Radiology and the American Radium Society, as well as numerous local societies.

A letter from Dr. P. F. Butler after Dr. Elward's death pays tribute to him and sums up his outstanding characteristics and qualities. It is quoted in part as follows: "I was very close to Joe and he was one of the men in whom I took a great deal of pride. Because of his outstanding success I was continually holding him up as an example to the younger interns in my department. He was an unusually dependable type of man, even as an intern. He accepted any detail assigned to him—even a disagreeable one—like a good soldier and saw it through to its finish. Perhaps outstanding of his traits was his courteous and respectful attitude toward his seniors, a trait seen all too little nowadays. With such a background it was inevitable that he should make a success of his private practice. He also held to the sound idea that we are physicians first and specialists next. This gave him the opportunity to make use of his wide knowledge of collateral medicine, thus greatly enhancing his value as a specialist. He showed his versatility in his writings and lectures, most of them original contributions. In his death our specialty loses another of its outstanding members."

Ramsay Spillman

SOCIETY PROCEEDINGS, CORRESPONDENCE AND NEWS ITEMS

Items for this section solicited promptly after the events to which they refer.

MEETINGS OF ROENTGEN SOCIETIES*

United States of America

American Roentgen Ray Society
Secretary, Dr. H. Dabney Kerr, University Hospital, Iowa City, Iowa. Annual Meeting: 1943, cancelled.

American College of Radiology
Secretary, Mac F. Cahal, 540 N. Michigan Ave., Chicago, Ill. Annual meeting: 1943, to be announced.

Section on Radiology, American Medical Association
Secretary, Dr. J. T. Murphy, 421 Michigan St., Toledo, Ohio. Annual meeting: 1943, cancelled.

Arkansas Radiological Society
Secretary, Dr. J. S. Wilson, Mack Wilson Hospital, Monticello, Ark. Meets every three months and also at time and place of State Medical Association.

Radiological Society of North America
Secretary, Dr. D. S. Childs, 607 Medical Arts Bldg., Syracuse, N. Y. Annual meeting: Drake Hotel, Chicago, Ill., Nov. 29–Dec. 3, 1943.

Radiological Section, Baltimore Medical Society
Secretary, Dr. Walter L. Kilby, Baltimore. Meets third Tuesday each month, September to May.

Section on Radiology, California Medical Association
Secretary, Dr. J. D. Coate, 434 Thirtieth St., Oakland, Calif.

Radiological Section, Connecticut Medical Society
Secretary, Dr. Max Climan, 242 Trumbull St., Hartford, Conn. Meets bi-monthly on second Thursday, at place selected by Secretary. Annual meeting in May.

Section on Radiology, Illinois State Medical Society
Secretary, Dr. H. W. Ackemann, 321 W. State St., Rockford, Ill.

Radiological Section, Los Angeles County Medical Association
Secretary, Dr. Donald R. Laing, 65 North Madison Ave., Pasadena, Calif. Meets on second Wednesday of each month at the County Society Building.

Radiological Section, Southern Medical Association
Secretary, Dr. Roy G. Giles, Temple, Texas.

Brooklyn Roentgen Ray Society
Secretary, Dr. Leo Harrington, 880 Ocean Ave., Brooklyn, N.Y. Meets monthly on fourth Tuesday, October to April.

Buffalo Radiological Society
Secretary, Dr. Joseph S. Gian-Francheschi, 610 Niagara St., Buffalo, N. Y. Meets second Monday of each month except during summer months.

Chicago Roentgen Society
Secretary, Dr. Warren W. Furey, 6844 S. Oglesby Ave., Chicago, Ill. Meets second Thursday of each month October to April inclusive at the Palmer House.

Cincinnati Radiological Society
Secretary, Dr. Samuel Brown, 707 Race St., Cincinnati, Ohio. Meets third Tuesday of each month, October to May, inclusive.

Cleveland Radiological Society
Secretary, Dr. J. O. Newton, 13921 Terrace Rd., East Cleveland. Meets at 6:30 P.M. at Midday Club on fourth Monday each month, October to April, inclusive.

Denver Radiological Club
Secretary, Dr. Edward J. Meister, 366 Metropolitan Bldg., Denver, Colo. Meets third Friday of each month at Denver Athletic Club.

Detroit Roentgen Ray and Radium Society
Secretary, Dr. E. R. Witwer, Harper Hospital. Meets monthly on first Thursday from October to May, at Wayne County Building.

Florida Radiological Society
Acting Secretary, Dr. Walter A. Weed, 204 Exchange Bldg., Orlando, Fla. Meetings in May and November.

Georgia Radiological Society
Secretary, Dr. James J. Clark, 478 Peachtree St., Atlanta, Ga. Meets in November and at annual meeting of Medical Association of Georgia in the spring.

Radiological Society of Kansas City
Secretary, Dr. Arthur B. Smith, 800 Argyle Bldg., Kansas City, Mo. Meets third Thursday of each month at a place designated by the president.

Illinois Radiological Society
Secretary, Dr. Wm. DeHollander, St. John's Hospital, Springfield, Ill. Meets three times a year.

Indiana Roentgen Society
Secretary, Dr. H. C. Ochsner, Methodist Hospital, Indianapolis. Meeting held the second Sunday in May annually.

Kentucky Radiological Society
Secretary, Dr. W. C. Martin, 321 W. Broadway, Louisville. Meets annually in Louisville on first Saturday in April.

Long Island Radiological Society
Secretary, Dr. Marcus Wiener, 1430-48th St., Brooklyn, N. Y. Meets Kings County Med. Soc. Bldg. monthly on fourth Thursday, October to May, 8:30 P.M.

Louisiana Radiological Society
Secretary, Dr. J. R. Anderson, 1130 Louisiana Ave., Shreveport. Meets annually during Louisiana State Medical Society Meeting.

Michigan Association of Roentgenologists
Secretary, Dr. E. M. Shebesta, 1429 David Whitney Bldg., Detroit. Three meetings a year, Fall, Winter, Spring.

Milwaukee Roentgen Ray Society
Secretary, Dr. C. A. H. Fortier, 231 W. Wisconsin Ave., Milwaukee, Wis. Meets monthly on second Monday at University Club.

Minnesota Radiological Society
Secretary, Dr. J. P. Medelman, 572 Lowry Medical Arts Bldg., St. Paul.

Nebraska Radiological Society
Secretary, Dr. D. A. Dowell, Medical Arts Bldg., Omaha, Nebr. Meets third Wednesday of each month, at 6 P.M. at either Omaha or Lincoln.

New England Roentgen Ray Society
Secretary, Dr. Hugh F. Hare, Lahey Clinic, Boston, Mass. Meets monthly on third Friday, Boston Medical Library.

Radiological Society of New Jersey
Secretary, Dr. H. J. Perlberg, 921 Bergen Ave., Jersey City. Meets annually at time and place of State Medical Society. Mid-year meetings at place chosen by president.

New York Roentgen Society
Secretary, Dr. M. M. Pomeranz, 1020 Park Ave., New York City. Meets monthly on third Monday, New York Academy of Medicine, at 8:00 P.M.

North Carolina Roentgen Ray Society
Secretary, Dr. Major Fleming, Rocky Mount, N. C. Annual meeting at time and place of State Medical Society. Mid-year scientific meeting at place designated.

North Dakota Radiological Society
Secretary, Dr. L. A. Nash, St. John's Hospital, Fargo. Meetings held by announcement.

Central New York Roentgen Ray Society
Secretary, Dr. C. F. Potter, 820 S. Crouse Ave., Syracuse. Three meetings a year. January, May, November.

* Secretaries of Societies not here listed are requested to send the necessary information to the Editor.

Ohio Radiological Society
Secretary, Dr. J. E. McCarthy, 707 Race St., Cincinnati. Meets at time and place of annual meeting of Ohio State Medical Association.

Pacific Roentgen Society
Secretary, Dr. L. H. Garland, 450 Sutter St., San Francisco, Calif. Meets annually, during meeting of California Medical Association.

Pennsylvania Radiological Society
Secretary, Dr. L. E. Wurster, 416 Pine St., Williamsport. Annual meeting, Brunswick Hotel, Lancaster, Pa., May 15–16, 1943.

Philadelphia Roentgen Ray Society
Secretary, Dr. R. P. Barden, University Hospital, Meetings first Thursday of each month from October to May inclusive at 8:15 P.M., in Thompson Hall, College of Physicians, 19 S. 22d St.

Pittsburgh Roentgen Society
Secretary, Dr. R. G. Alley, 4800 Friendship Ave. Meets second Wednesday each month, 4:30 P.M., October to June, Pittsburgh Academy of Medicine.

Rochester Roentgen Ray Society, Rochester, N. Y.
Secretary, Dr. Sidney Larson, Strong Memorial Hospital. Meets monthly on third Monday from October to May, inclusive, 8 P.M. at Strong Memorial Hospital.

Rocky Mountain Radiological Society
Secretary, Dr. A. M. Popma, 220 N. First St., Boise, Idaho.

St. Louis Society of Radiologists
Secretary, Dr. P. C. Schnoebelen, 462 N. Taylor Ave. Meets fourth Wednesday of each month, except June, July, August, and September, at a place designated by the president.

San Francisco Radiological Society
Secretary, Dr. H. A. Hill, 450 Sutter St., San Francisco. Meets monthly on third Thursday at 7:45 P.M., first six months at Toland Hall, second at Lane Hall.

Shreveport Radiological Club
Secretary, Dr. R. W. Cooper, Charity Hospital, Shreveport, La. Meets monthly on third Wednesday, at 7:30 P.M., September to May inclusive.

South Carolina X-Ray Society
Secretary, Dr. T. A. Pitts, Baptist Hospital, Columbia, S. C. Meets in Charleston on first Thursday in November, also at the time and place of South Carolina State Medical Association.

Tennessee Radiological Society
Secretary, Dr. J. M. Frère, 707 Walnut St., Chattanooga, Tenn. Meets annually at the time and place of the Tennessee State Medical Association.

Texas Radiological Society
Secretary, Dr. Herman Klapproth, Sherman, Texas.

University of Michigan Department of Roentgenology Staff Meeting
Meets each Monday evening from September to June, at 7 P.M. at University Hospital.

University of Wisconsin Radiological Conference
Secretary, Dr. E. A. Pohle, 1300 University Ave., Madison, Wis. Meets every Thursday from 4:00–5:00 P.M., Room 301, Service Memorial Institute.

Virginia Radiological Society
Secretary, Dr. E. L. Flanagan, 116 E. Franklin St., Richmond, Va. Meets annually in October.

Washington State Radiological Society
Secretary, Dr. K. J. Holtz, American Bank Bldg., Seattle. Meets fourth Monday each month, College Club, Seattle.

X-ray Study Club of San Francisco
Secretary, Dr. J. M. Robinson, University of California Hospital. Meets monthly in evening on third Thursday.

Cuba

Sociedad de Radiología y Fisioterapia de Cuba
President, Dr. J. Manuel Viamonte, Hospital Mercedes, Habana, Cuba. Meets monthly in Habana.

British Empire

British Institute of Radiology Incorporated with the Röntgen Society
Meets monthly on third Thursday from November to June inclusive, at 8:15 P.M., 32 Welbeck St., London.

Section of Radiology of the Royal Society of Medicine (Confined to Medical Members)
Meets on the third Friday of each month during the winter at 8:15 P.M. at the Royal Society of Medicine 1, Wimpole St., London, W. 1.

Faculty of Radiologists
Secretary, Dr. M. H. Jupe, 32 Welbeck St., London, W. 1 England.

Section of Radiology and Medical Electricity, Australasian Medical Congress
Secretary, Dr. H. M. Cutler, 139 Macquarie St., Sydney, New South Wales.

Radiological Section of the Victorian Branch of the British Medical Association
Secretary, Dr. Keith Hallam, St. George's Hospital, K.E.W., Melbourne, E. 4, Victoria, Australia. Meets monthly from March to November inclusive.

Canadian Association of Radiologists
Secretary, Dr. A. D. Irvine, 540 Tegler Bldg., Edmonton, Alberta.

Section of Radiology, Canadian Medical Association
Secretary, Dr. C. M. Jones, Inglis St., Ext. Halifax, N. S.

Radiological Section, New Zealand British Medical Association
Secretary, Dr. Colin Anderson, Invercargill, New Zealand. Meets annually.

Continental Europe

Sociedad Espanola de Radiologia y Electrologia
Secretary, Dr. J. Martin-Crespo, Fuencarral, 7. Madrid, Spain. Meets monthly in Madrid.

Société Suisse de Radiologie (Schweizerische Röntgen-Gesellschaft)
Secretary for French language, Dr. A. Grosjean La Chaux de Fonds.
Secretary for German language, Dr. Scheurer, Molzgasse Biel. Meets annually in different cities.

Societatea Romana de Radiologie si Electrologie
Secretary, Dr. Oscar Meller, Str. Banul Mărăcine, 30, S. I., Bucuresti, Roumania. Meets second Monday in every month with the exception of July and August.

All-Russian Roentgen Ray Association, Leningrad: USSR in the State Institute of Roentgenology and Radiology, 6 Roentgen St.
Secretaries, Drs. S. A. Reinberg and S. G. Simonson. Meets annually.

Leningrad Roentgen Ray Society
Secretaries, Drs. S. G. Simonson and G. A. Gusterin. Meets monthly, first Monday at 8 o'clock, State Institute of Roentgenology and Radiology, Leningrad.

Moscow Roentgen Ray Society
Secretaries, Drs. L. L. Holst, A. W. Ssamygin and S. T. Konobejevsky. Meets monthly, first Monday, 8 P.M.

Scandinavian Roentgen Societies
The Scandinavian roentgen societies have formed a joint association called the Northern Association for Medical Radiology, meeting every second year in the different countries belonging to the Association.

WAR CONFERENCE

The medical, surgical and industrial hygiene experts who are so ably safeguarding the well-being of more than 20 million industrial workers have agreed to pool their knowledge and exchange their experiences regarding the many new and complex problems of today's wartime production. For this purpose their organizations—

The American Association of Industrial Physicians and Surgeons,

The American Industrial Hygiene Association, and

The National Conference of Governmental Hygienists—are combining their annual meetings in a four-day "War Conference" at Rochester, New York, May 24–27, 1943. Among the problems to be discussed from a practical standpoint are:

The mass entry of women into industry;

Older-age employees, with their various associated problems; proper placement and employability considerations of the 4-F rejectees;

Rehabilitation and proper employment of those already discharged from the military services because of disabling conditions;

Toxic and other hazards from new substances, new processes, and the use of substitute materials;

Absenteeism; fatigue; nutrition;

Effects of long hours; double shifts; two-job workers; overtime; increased industrial accident rates;

Advances in the treatment of illnesses and injuries, and many others.

This joint meeting will be a report on the state of the nation, by the men who know, in matters of industrial health. Dr. William A. Sawyer, Medical Director of Eastman Kodak, is General Chairman; Dr. James H. Sterner and Lieut. Comm. J. J. Bloomfield are arranging the programs for the industrial hygienists.

Physicians and surgeons, hygienists, engineers, nurses, executives—all who are interested in the problems of industrial health and their solution—are invited to attend as many of the sessions as they can arrange for; no registration fee is required

BOOK REVIEWS

Books sent for review are acknowledged under: Books Received. This must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interest of our readers as space permits.

THE DOCTORS MAYO. By H. B. Clapesattle. Cloth. Price, $3.75. Pp. 822, with numerous illustrations. Minneapolis: University of Minnesota Press, 1941.

This large volume is packed with history, recollections and romance. It is a human document. It is a history of the progress and advance of medicine and surgery for the past fifty years. The reader can open the volume anywhere and find fascinating and absorbing pages that identify some element in the development of the most successful and the most original system of integrated medical practice in the whole world. It may be that private enterprise as exemplified in the Mayo Clinic can never be duplicated or extended to this or other countries. Imitations have been ventured and maintained periods of success that were usually measured by the active life span of the leader. The story of the Doctors Mayo shows an undefinable breadth of fundamental sincerity, an undeniable urge to develop along sound, conservative lines, an unlimited ambition to add only able minds, a magnificent courage and confidence in the triumph of righteous effort; in fact, it is impossible to catalogue the many virtues that have contributed to the flowering of institutions and the influences of the Doctors Mayo.

This is probably the greatest success story in the annals of medicine. To the reviewer who made his first pilgrimage to Rochester thirty-five years ago, and met the older Mayo, this record of the Mayo saga becomes a vital document. However, it is inconceivable that any reader could be disappointed in the slowly expanding drama of American surgery as it is personalized by word and photograph from page to page.

There have been innumerable reviews of this interesting book and every one seems to be tinctured with personal recollections of the reviewer. There seems to be no reason why this one should not continue the idea, for every radiologist feels more or less of a proprietary interest in the successful career of radiology at the Mayo Clinic. One remembers the erratic Selby, although this book mentions Dr. J. Grosvenor Cross as the Rochester pioneer roentgenologist who later moved to Minneapolis. The renowned Carman came in 1912 after a brief interlude of the enthusiastic Vernon J. Willey. Carman brought Albert Miller with him from St. Louis as a sort of Boswell or alter ego. This team was given unlimited scope and they proceeded to gather statistics and establish diagnostic values, especially in gastrointestinal roentgenology. Aside from their contributions to roentgen diagnosis the several radiologists at Rochester have been extremely popular with their colleagues throughout the world. The personalities of Carman, Moore, Sutherland, Miller, Camp and Kirklin would probably have carried them far even without the glamour of the Rochester setting. They did take advantage of their unusual opportunities and have shared the harvest of roentgen lore generously.

Therapeutic radiology has been obliged to fight for every inch of acceptance at Rochester. The atmosphere has been surgical in spite of the breadth of vision and the practical approach to a complete medical and surgical service, adorned by research and plumed with graduate instruction. The department of Radium Therapy has been carried on, among others, by Leda J. Stacy, the modest and industrious Bowing and the statistical Fricke. These three have been concerned with pelvic conditions while New and Figi were more interested in radium therapy of the head and neck. Roentgen therapy seems to pursue a conservative course through the scholarly, inquisitive Desjardins, ably seconded by Leddy, Popp and Fear.

Dr. Will Mayo was always most cordial to radiologists and radiological organizations when they visited Rochester. Dr. Charles Mayo indulged in conducting roentgen examinations when Dr. Cross went to Minneapolis, and bore some scars of exposure upon his fingers. As testimony of the appreciation that Dr. Will Mayo had for roentgenology one recalls his welcoming remarks when the American Roentgen Ray Society spent a day at Rochester. To emphasize the tremendous values of visual adjuncts to medicine, he told of his visit to "the Victoria

Hospital in New Castle-on-Tyne where the surgeon, Rutherford Morrison, had printed upon the wall of his operating amphitheater facing the students the following five words 'Sight' in large letters; 'Touch' in smaller letters; 'Hearing' in still smaller letters; 'Smell' in fine print and, last, 'Taste' in print so small as to be hardly distinguishable across the room, this indicating Rutherford's estimation of the five special senses in relation to surgery." Dr. Will Mayo turned this recollection into a neat tribute to the visualized possibilities of the roentgen examination.

It is easy to recollect discussions among both admiring and critical visitors who wondered about the possible perpetuation of what started out to be only a surgical mecca. This volume gives some credit to Frank Billings for his advice to Dr. Will to expand the Clinic's base and cover the whole water front of medicine, surgery and the specialties. Not only has this been done but all avenues of graduate instruction, university alliance, research and allied sciences have been dovetailed into a panoramic institution that dominates the landscape of southern Minnesota. The integral human units that are now part and parcel of the whole have become important cogs in the organizations of medicine and in the medical literature of the whole world.

There will always be a Washington Monument as long as our American Democracy survives and there will always be a Mayo Clinic at Rochester as long as the ideals and the visions of the Doctors Mayo prevail in the councils of the staff organization. Things that are conceived within the minds of men and built by the hands of men can never be as permanent as the wonders of the earth. But there has never been another isolated spot on the face of the earth that has attracted more patients and more physicians and influenced both so successfully as the prairie village of Rochester with its native sons, The Doctors Mayo.

E. H. Skinner

Roentgen Technique. By Clyde McNeill, M.D., Louisville. Second edition. Cloth. Price, $5.00. Pp. 329, with 276 illustrations. Springfield, Illinois: Charles C Thomas, 1941.

This practical volume deals with roentgen-ray anatomy and positioning for roentgenography.

As in the first edition, we are impressed by the excellent manner in which the various standard positions have been described by photographs and line drawings, as well as an accompanying discussion of the projection on the opposite page. To this new second, somewhat enlarged edition, the author has added material on some of the newer procedures, making the volume more complete and comprehensive. The addition of certain references to the literature in some of the special procedures is to be particularly commended.

We recommend this book as one of the best constructed, handy manuals for ready reference that is available at the present time.

Paul C. Swenson

Nutrition and Chemical Growth in Childhood. Volume I. Evaluation. By Icie G. Macy, Ph.D., Director, Research Laboratory, Children's Fund of Michigan, Consultant for Nutrition to the Pediatric Staff of the Children's Hospital of Michigan; Member of the Food and Nutrition Board of the National Research Council, etc. With a Foreword by Hugo A. Freund, M.D., President Board of Trustees, Children's Fund of Michigan. Cloth. Price, $5.00. Pp. 432, with 66 illustrations. Springfield, Illinois: Charles C Thomas, 1942.

This is the first of two volumes written by Icie G. Macy, Director of the Research Laboratory, Children's Fund of Michigan, which presents a summary of an intensive clinical and biochemical investigation of normal children. Volume I, the subject of this review, has the title "Evaluation"; the second volume with the title "Interpretation" will appear in 1943 and will give the results of a continuation of the previous study. The first volume deals particularly with a discussion of clinical examination and developmental records, with biochemical methods, with dietetic and metabolic balance studies and with the average retentions of eighteen food constituents by normal children during many five day balance periods.

The most important aspect of the publication is a summary of balance studies of eighteen different chemical substances in normal children in conjunction with other observations which may be classified as pediatric, anatomic, psychometric, physiologic, anthropometric, roentgenologic and chemical. It is stressed that when the rapid polarographic and spectrographic methods for the determination of substances in biologic material are employed, the results can be made available within a few days after the

termination of the series of observations. These newer methods, according to the author, should be of great practical value in clinical medicine and pediatrics.

No attempt can be made by the reviewer to evaluate the results which appear to be derived from a most careful, thorough and painstaking extended study of normal children, in which all modern methods of study are applied. Conclusions concerning the following are presented: the feeding of recommended allowances, the variability of food stuffs, the basal metabolism, and energy utilization, chemistry of the formed elements of the blood, evaluation of skeletal maturation, roentgenographic gastrointestinal studies, and the accurate sampling of food, urine and feces.

In addition to a study of the total energy exchange, the results of a metabolic balance studies on the following substances are given: nitrogen, calcium, magnesium, sodium, potassium, sulfur, chlorine, phosphorus, copper, zinc, iron, nickel, carbon, fat and complex carbohydrates.

The material presented represents a huge undertaking which has had the extensive cooperation of a large number of individuals. The Trustees of the Children's Fund of Michigan, Dr. Macy, and her associates should be congratulated on the completion of such an important and comprehensive project. The book is an excellent summary of the most important phases of nutrition and growth in childhood and should serve as an excellent and reliable reference text. It should also be of great value to those engaged in nutritional investigations relating to childhood and to all physicians engaged in the care of children.

Cyrus C. Sturgis

Diseases of the Nails. By V. Pardo-Castello, M.D., Assistant Professor of Dermatology and Syphilology, University of Havana, Member of the American Dermatological Association, etc. With a Foreword by Howard Fox, M.D., Professor of Dermatology and Syphilology, New York University, University and Bellevue Hospital Medical College. Second edition. Cloth. Price, $3.50. Pp. 193, with 98 illustrations. Springfield, Illinois: Charles C Thomas, 1941.

This book presents the subject of diseases of the nails in a concise and comprehensive manner. In addition to the text there are 98 excellent illustrations that give the reader a pictorial representation of many conditions affecting the nails. For the radiologist and general practitioner who often receive complaints from patients concerning nail affections, this book offers an opportunity for an intelligent approach to diagnosis and therapy. This book should be in every doctor's library, and in many instances it will be referred to daily.

The author has collected the material for the book not only from his large practice, but from many others interested in this important subject. The publisher, as usual, has prepared a book in which the type, the paper, the illustrations and the binding are excellent in all details.

Eugene P. Pendergrass

Surgical Physiology. By Joseph Nash, M.D., Assistant Professor of Clinical Surgery, New York University College of Medicine; Associate Visiting Surgeon, Bellevue Hospital, New York City; First Lieutenant, Medical Corps, U. S. Army; Assistant Chief of the Surgical Service, Lovell General Hospital, Fort Devens, Massachusetts. Cloth. Price, $6.00. Pp. 496, with 16 illustrations. Springfield, Illinois: Charles C Thomas, 1942.

This book is essentially a condensed text of practical mammalian physiology. It is less detailed and contains fewer illustrations than the earlier physiology texts that were written with the view of correlating basic physiology with clinical medicine. It has as its basis a series of lectures given by the author since 1930 at the New York University College of Medicine as a part of the Graduate Course in Surgery.

The amount of condensation that this work required evidently necessitated the sacrifice of the principle of logical sequence in the secondary structure of the work; as a consequence the reader finds it difficult to retain what he reads.

Critical reading uncovers many contextual contradictions. This is especially true in the chapters on the circulation, surgical shock and respiration. The contradictions that appear are somewhat proportional to the number of primary sources from which the material was drawn. The chapter on the kidney is very well written and the chapters on acid base balance, salt and water balances and the hormones are good. These chapters may well be worth the price of the book.

The text lacks an organized reference to the

physiology of anesthesia. Without a doubt, anesthesia exerts a very great influence upon the integration of physiological processes and consequently any text of "Surgical Physiology" cannot be complete without a discussion of the effects of anesthesia upon physiological processes.

The basic physiologic principles governing growth and repair are also neglected. The reviewer feels that as a consequence the author has missed a golden opportunity for the construction of an interesting and enlightening introduction that could have contained some philosophical consideration of the problems confronting the physiologist and the surgeon. This might have served to make the book a challenge to thought rather than the challenge to memory that it is.

Whatever the faults of the text may be, it is directed toward filling a need that every surgeon knows to be existent but is one that seemingly only can be filled in a satisfactory manner by a collective effort of experienced surgeons and highly trained and experienced physiologists.

It is unlikely that any one man will ever be capable of acquiring a mastery of the ramified and complex divisions of physiology and of surgery that would enable him to write a critically constructed text of "Surgical Physiology."

Should this book stimulate the collaboration of specialists in the fields of physiology and of surgery in writing a comprehensive text, it will have provided of invaluable service.

Frederick A. Coller

Directory of Medical Specialists Certified by American Boards, 1942. Compiled by the Advisory Board for Medical Specialties. Cloth. Price, $7.00. Pp. 2495. New York: Columbia University Press, 1942.

As most physicians know, this Directory is the only official and complete list of medical specialists. It lists them geographically as well as alphabetically and gives not only their professional biographies but in addition full details of special training leading to certification.

While the first edition had a large circulation, being widely used in business and medical organization offices, as well as by individual physicians, it is now obsolete because of the large number of diplomates certified since 1939 by the former boards and also by the addition of Boards of Anesthesiology, Plastic Surgery and Neurological Surgery.

The size of the volume has been increased 50 per cent although 4,000 added names account for about a 30 per cent increase. The disproportion is accounted for by the additional biographical data, this having been amplified both as to past positions, such as internships, new appointments, and military service. Procurecurement and selective service officials find it very helpful in identifying applicants for commissions and verifying their qualifications.

In these strenuous times few can afford to be without the aid of such a useful book.

E. Walter Hall

BOOKS RECEIVED

An X-Ray Atlas of Silicosis. By Arthur J. Amor, M.D. (Lond.), M.Sc. (Wales), Honorary Physician, Clydach Memorial Hospital; Medical Officer, Mond Nickel Co., Ltd., Swansea. The legends translated into French by Robert E. Horne, M.A. (Wales), Medical Secretary, Mond Nickel Co., Ltd., Swansea. With a Foreword by Sir Wilson Jameson, M.A., M.D. (Aberdeen), F.R.C.P. of the Middle Temple, Barrister-at-Law; Dean of the London School of Hygiene and Tropical Medicine. Cloth. Price, $8.00. Pp. 206, with 72 illustrations. Baltimore: Williams & Wilkins Company, 1941.

The 1941 Year Book of Radiology. *Diagnosis*, Edited by Charles A. Waters, M.D., Associate in Roentgenology, Johns Hopkins University; Assistant Visiting Roentgenologist, Johns Hopkins Hospital; Associate Editor, Whitmer B. Firor, M.D., Assistant in Roentgenology, Johns Hopkins University; Assistant in Roentgenology, Johns Hopkins Hospital. *Therapeutics*, Edited by Ira I. Kaplan, B.Sc., M.D., Director, Radiation Therapy Department, Bellevue Hospital, New York City; Associate Radiologist, Lenox Hill Hospital, New York City; Clinical Professor of Surgery, New York University Medical College. Cloth. Price, $5.00. Pp. 440, with 486 illustrations. Chicago: Year Book Publishers, Inc., 1941.

Intestinal Obstructions: A Physiological and Clinical Consideration with Emphasis on Therapy; Including Description of Operative Procedures. By Owen

H. Wangensteen, B.A., M.D., Ph.D., Professor of Surgery of the University of Minnesota and Surgeon-in-Chief of the University of Minnesota Hospital. Second Edition. Cloth. Price, $7.00. Pp. 484, with 143 illustrations. Springfield, Illinois: Charles C Thomas, 1942.

Plastic Surgery of the Breast and Abdominal Wall. By Max Thorek, M.D., LL.D., F.I.C.S., F.I.C.A., K.L.H. (France); K.C.I.; C.O. St. Alex; Medal of Hon. Rep. of Venezuela; Professor of Surgery, Cook County Hospital; Consulting Surgeon, Municipal Tuberculosis Sanitarium, Chicago; Surgeon-in-Chief, American Hospital of Chicago, etc. With an Introduction by Rudolf Nissen, M.D., F.I.C.S., Formerly Associate Professor of Surgery of the University of Berlin, and Professor and Head of the Department of Surgery of the Medical University of Istanbul, Turkey. With a Foreword by J. Eastman Sheehan, M.D., F.A.C.S., Professor of Plastic Reparative Surgery, New York Polyclinic; Surgeon, Morrisania City Hospital, New York; Associate Surgeon and Lecturer, International Clinic, Lariboisiére Hospital, Paris, France. Cloth. Price, $16.50. Pp. 446, with 458 illustrations. Springfield, Illinois: Charles C Thomas, 1942.

Nutrition and Chemical Growth in Childhood. Volume I. Evaluation. By Icie G. Macy., Ph.D., Director, Research Laboratory, Children's Fund of Michigan, Consultant for Nutrition to the Pediatric Staff of the Children's Hospital of Michigan; Member of the Food and Nutrition Board of the National Research Council, etc. With a Foreword by Hugo A. Freund, M.D., President Board of Trustees, Children's Fund of Michigan. Cloth. Price, $5.00. Pp. 432, with 66 illustrations. Springfield, Illinois: Charles C Thomas, 1942.

Occupational Tumors and Allied Diseases. By W. C. Hueper, M.D., Assistant Director and Principal Pathologist, Warner Institute for Therapeutic Research, New York City. Cloth. Price, $8.00. Pp. 896. Springfield, Illinois: Charles C Thomas, 1942.

A Manual of Radiotherapy. By Murray M. Friedman, M.D., Assistant Professor of Radiology, College of Physicians and Surgeons, Columbia University; Assistant Radiologist, Presbyterian Hospital, New York, N. Y. Paper. Price, $1.50. Pp. 86, with 30 illustrations. Ann Arbor, Michigan: Edwards Brothers, Inc., 1942.

Protection of Radium During Air Raids. National Bureau of Standards Handbook H38. Issued by the U. S. Deparment of Commerce, National Bureau of Standards. Paper. Price, 10 cents. For sale by the Superintendent of Documents, Washington, D. C. Pp. 17, with 3 illustrations. Washington, D. C.: United States Government Printing Office, 1942.

Directory of Medical Specialists Certified by American Boards, 1942. Compiled by the Advisory Board for Medical Specialities. Cloth. Price, $7.00. Pp. 2495. New York: Columbia University Press, 1942.

DEPARTMENT OF TECHNIQUE

Department Editor: Robert B. Taft, M.D., B.S., M.A., 103 Rutledge Ave.
Charleston, S. C.

DUPLICATION OF ROENTGENOGRAMS BY THE LIGHT REVERSAL PROCESS*

By GEORGE C. HENNY, M.D., GUSTAVUS C. BIRD, JR., M.D., *and*
HERBERT M. STAUFFER, M.D.
PHILADELPHIA, PENNSYLVANIA

IT IS well known among news photographers that a negative can be made from another negative by the light reversal process. In other words, negatives can be directly duplicated. We have been surprised to find how few roentgenologists are aware of this process which can be used also with roentgenographic film so as to duplicate roentgenograms. Duplicates of roentgenograms can be made very conveniently. Special film and developer are not required, and the process, which is described below, is so simple that anyone can do it. The only special piece of equipment required is an ordinary photographer's printing frame large enough to hold the film to be copied.

The roentgenogram which is to be duplicated is placed on the clean glass of the printing frame. On top of this, in the darkroom, is placed an ordinary unexposed roentgenographic film of the same size. The printing frame is then closed, thereby clamping the unexposed film tightly against the roentgenogram. The glass of the printing frame may then be covered with a piece of black paper, carried outside or to an *open* window (without fly screen on it) and there exposed directly to the sunlight for about thirty seconds. The printing frame is taken to the darkroom and the film is given standard development. When completely processed, the film will be a close duplicate of the original. The time of exposure to the sunlight will depend somewhat on the time of the day and the clearness of the atmosphere, and also upon the general density of the film to be duplicated. Since there is a great deal of latitude in this process, the exposure does not have to be carefully made, and thirty seconds is a good starting point. If the resulting film is too dark, the exposure to the light should be increased, and if it is too light, it should be decreased. This is the opposite of ordinary photographic procedure because of the reversal process. If the sun is not shining when the duplications have to be made, it is possible to use artificial light, but the results may not be quite as good. In this case perhaps the simplest procedure is to place the printing frame with the roentgenogram and underlying film directly against the glass of a film illuminator. The exposure time depends on the brightness of the illuminator but in most cases ten or fifteen minutes will be required. The film is developed in the darkroom in the usual manner, and the result should be a close duplicate of the original. If the light intensity over the surface of the illuminator is not uniform, the duplicate will show this unevenness.

A fair duplication can be made by exposing the film 20 inches below a 100 watt light for thirty minutes. This film will probably be darker than the original but will have good diagnostic detail.

To show the progress of the reversal process, a roentgenogram was made of an aluminum stepladder. The exposure was

* From the Department of Radiology, Temple University Hospital, Philadelphia.

so chosen that the range of photographic densities was between 0.5 and 2.2 as shown by the broken line of Figure 1. This film was then duplicated, using Eastman Blue Brand roentgen film, by exposure to the sunlight for 0.2, 1, 3, 10 and 30 seconds. The duplicates thus exposed were measured with a densitometer and the data were obtained for the curves of Figure 1. Here it is seen that the longer the exposure, the less dense is the resulting film after development. Thus at 0.2 second (this exposure could not be accurately timed) the film is very black throughout the whole range, and it is evident that there is very little contrast. As the exposure to the sunlight is increased, it is found that at thirty seconds the density curve is nearly superimposed throughout the whole density range on the curve of the original. This shows that a nearly exact duplicate can be made, as far as density is concerned. The fineness of detail suffers slightly, due undoubtedly to the fact that the films are the double emulsion type. Bone trabeculations can easily be seen on the duplicate film so that if the original film and its duplicate are placed side by side and viewed at the usual distance, very little difference between the two can be observed.

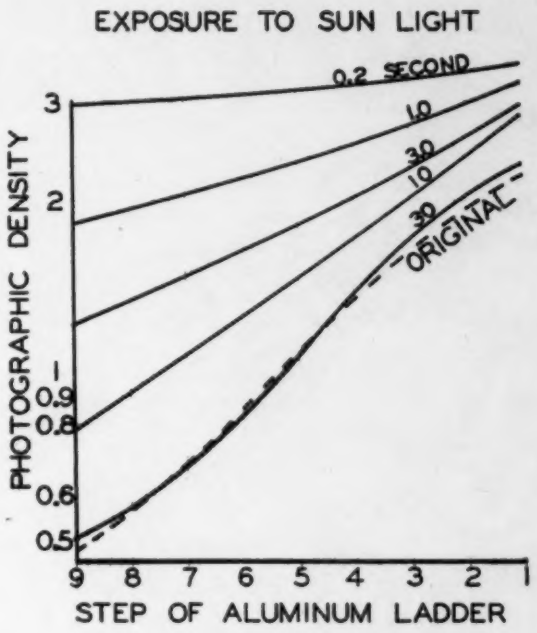

Fig. 1. Photographic density curves of duplicates of a roentgenogram of an aluminum stepladder. The original roentgenogram, having nine density steps, is represented by the broken line curve. The copies of the original were made by printing it on Eastman Blue Brand roentgen film, exposure being made to the morning sun for the times indicated on each curve. The films were developed in the usual manner in Eastman Kodalk X-Ray Developer for six minutes at 65° F.

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ABSTRACTS OF ROENTGEN AND RADIUM LITERATURE

ROENTGEN AND RADIUM THERAPY

Spangler, Davis. The effect of x-ray therapy for closure of the epiphyses: preliminary report. *Radiology*, Sept., 1941, *37*, 310–315.

There are various causes for unequal length of the legs. Orthopedic lengthening of the short leg requires months of hospitalization and surgical shortening of the long one is usually objected to. The author suggests closing of the epiphyses at the knee of the long leg, preventing further growth and allowing the shorter leg to catch up. This is a preliminary report to suggest further trial of the method, as he has only used it in 4 cases, which are described. The treatment was successful in 3 cases and failed in the fourth. He believes that about 3,000 r given in one fractionated series will bring about closure of the epiphyses. He irradiates through four portals, one anterior, one posterior and one on each side, giving 750 r to each with 140 kv., through 0.25 mm. copper. The fractionating is arranged so as to produce tanning but not epidermitis. The knee joint cartilages should be protected with lead strips.

These children were treated just before the spurt of bone growth that takes place at puberty. He thinks the results would be more satisfactory if they were treated at six to ten years of age.—*Audrey G. Morgan.*

Baird, L. W. Roentgen irradiation of calcareous deposits about the shoulder. *Radiology*, Sept., 1941, *37*, 316–324.

The author discusses the roentgen treatment in 18 cases of calcified subacromial bursitis. In diagnosis two exposures should be made, one with external rotation of the humerus and one with internal rotation. As the deposits may be bilateral it is best to make exposures of both shoulders, even though the pain may be bilateral. In very acute cases it is often necessary to use a soft tissue technique as the shadows of the deposits are very faint.

Of this series of cases 9 were acute, 5 subacute and 4 chronic. The technique was as follows: 300 r (measured in air) in a single dose through a 15×15 cm. cone angled slightly toward the body over the anterolateral portion of the shoulder: 200 kv., constant potential, 1.0 mm. copper plus 1.0 mm. aluminum filter, 50 cm. distance, 18 ma. Only one exposure was necessary to relieve pain and restore function in all of the acute and 2 of the subacute cases. In the 3 other subacute cases two treatments were necessary. Two of the chronic patients were relieved by three treatments at intervals of four weeks while the treatment was a failure in the other two. This method is not adapted for the treatment of chronic cases in which the chief symptom is limitation of motion. This is caused by fibrosis and adhesions and is not relieved by irradiation.—*Audrey G. Morgan.*

Klein, I., and Klemes, I. S. Treatment of peritendinitis calcarea in the shoulder joint. *Radiology*, Sept., 1941, *37*, 325–330.

The authors give a tabulation of their cases of peritendinitis calcarea of the shoulder joint from 1932 to 1940. Physiotherapy in the form of infra-red therapy and diathermy was used from 1932 to 1937 while roentgen irradiation was used from 1937 to 1940. The roentgen technique was as follows: 75 to 100 r in air every three to seven days for four doses. If necessary a second course was given after a month's rest. The physical factors were: 125 kv., 4.0 mm. aluminum filter, 5 ma., 30 cm. distance, field 8×8 cm., or 180 kv., 4 ma., 40 cm. distance, 0.5 mm. copper and 1.0 mm. aluminum filter, field 10×10 cm. The choice of method depended on the thickness of the shoulder. Both gave the same results. The calcifications disappeared under roentgen treatment and the period of disability was greatly shortened as compared to that with physiotherapy. The average period of disability with physiotherapy was fifty days, with roentgen treatment ten days. Seven illustrative cases are described and illustrated with roentgenograms.—*Audrey G. Morgan.*

Stone, Robert S., and Robinson, J. Maurice. Roentgen irradiation of the pelvis in carcinoma of the cervix uteri. *Radiology*, May, 1941, *36*, 521–533.

In the authors' plan of treatment radium is used for the primary lesion in the cervix and

roentgen irradiation is used for the treatment of the territories to which the lesion is apt to spread. If the tumor of the cervix is small and well localized a complete course of radium treatment is given. If the tumor is in Stage I or II this is followed by a Wertheim operation; if it is more advanced roentgen treatment is given. But if the growth is large and extensive, roentgen treatment is given first in an attempt to decrease its size, and radium treatment is given two to six weeks later.

Ninety per cent of lymphatic involvement occurs in the primary lymph nodes, which must therefore be irradiated. These are the hypogastric, the obturator, the iliac, the sacral and the parametral nodes. The cancer may extend directly into the parametrium and the vagina and these must be included in the fields to be irradiated.

The fields to be irradiated should be marked out carefully and the beam should be directed not at the cervix but at the lateral walls of the true pelvis and the anterior surface of the sacrum. The object is to irradiate not a certain area of skin but the structures lying beneath it and the physician himself should attend to the placing of the patient and the direction of the beam. This should never be left to technicians for it is a medical and not a technical problem. The amount of irradiation given should be as much as the normal tissues will bear.

The authors have found that six fields, two anterior, two posterior, and two lateral, give the best internal distribution of the irradiation.

They compare the results in two series of cases in the first of which they used 200 kv. therapy, half-value layer 1.05 mm. copper in which one anterior and one posterior field 20×20 cm. and two lateral fields 10×20 cm. were used. The total dosage rarely exceeded 2,000 r, in air, per field. In the second series they used 1,000 kv., with anterior and posterior fields 20×20 cm. but no lateral fields; at first 316 r and later 240 r, in air, was used per field per treatment. There was a higher percentage of survivals in the group treated with 200 kv., but there was evidence in both that the growth of the cancer was slowed or stopped by the roentgen treatment.—*Audrey G. Morgan.*

Cantril, Simeon T., Buschke, Franz, and Parker, H. M. Irradiation in cancer of the cervix uteri. *Radiology*, May, 1941, *36*, 534–542.

In treating cancer of the cervix an attempt should first be made to determine the anatomic limits of the growth and the effect it has had on the patient. As the majority of deaths are due to occlusion of the ureters, cystoscopy and intravenous urography must be used in many cases. Among 19 Stage IV cases in which intravenous urography was done half showed some degree of ureteral obstruction.

The authors do not give purely palliative treatment, for the amount of palliation obtained is rarely in proportion to the severity of the treatment. Patients with ureteral obstruction are treated with the object of restoring permeability of the ureter if possible. They follow no rigid outline of treatment as this is a disease in which individualization is most important. In all except Stage I cases they supplement radium treatment with roentgen irradiation, using 800 kv., 10 ma., 4 mm. lead filtration, 100 cm. distance, with an intensity of 23.5 r per minute for a field of 10×14 cm. Types of radium applicators are shown. As a rule they give a total radium dose of about 8,000 mg-hr., equivalent to about 4,500 r. Radium should be given first, followed by roentgen irradiation unless anatomical conditions make this method impossible. A rectal reaction can hardly be avoided if sufficient treatment is given. They use two anterior suprapubic and two posterior lumbosacral fields, and if greater dosage to the parametrium is desirable also two oblique ischiosciatic fields. The size of the fields is 10×10 cm. in small patients and 10×14 cm. in larger ones.

Isodose curves were determined in a pressdwood model of the pelvis of a living subject. A study of these measurements shows that a roentgen-ray dose of 2,600 r contributes little to the combined dosage at the periphery of the broad ligaments in a broad pelvis. It is known clinically that roentgen therapy rarely cures a cancer of the cervix that has spread into the broad ligaments and to the wall of the pelvis. They show also that the effective range of radium is sufficient for Stage I and that in Stage II the roentgen-ray contribution is not apt to increase the dosage beyond the tolerance level. In Stage III an increase of either the radium or roentgen-ray dose may be necessary to control outlying metastases. In patients with a small pelvis this is best obtained by increasing the radium dosage and in patients with a large pelvis the roentgen-ray doses may be increased with greater safety than in smaller ones, though

wherever radium can be used its effects can more readily be localized in the places where it is most needed and normal tissues are injured less.

Radium is the more important source of radioactivity and the success of its use should not be endangered by using external roentgen treatment first and carrying it to the limit of tolerance of the normal tissues. In Stage IV in which radium cannot be used the curability cannot be increased solely by increasing dosage by supervoltage therapy. There are other factors than dosage to be considered; the biologic effects of radiation on normal and malignant tissues are of the first importance. For certain kinds of cells there is no lethal dose and there is no certainty that tissues will be destroyed by any given irradiation.—*Audrey G. Morgan.*

Liljencrantz, Eric, and Newell, R. R. Technic of irradiation of cancer of the uterine cervix, combining radium and supervoltage roentgen rays. *Radiology*, May, 1941, *36*, 543–549.

For the past few years the authors have been using very hard roentgen irradiation (half-value layer = 2.7 mm. Sn). They use three fields at 120 degrees, one suprapubic and two posterolateral (gluteal). The fields are 15 to 16 cm. circles. A sketch is given showing the entrances and exits. As external irradiation alone cannot give a third of the dosage at the cervix attained by radium, radium treatment is added. They believe that roentgen irradiation should be used first and radium afterward. They treat patients six days a week with rotation of the three fields. The posterior areas are generally given 400 r each time and the suprapubic area 300 r. Backscatter adds 20 per cent. In a month the limits of skin tolerance will have been reached with 3,600 r tissue dose in front and 4,800 r gluteal. Radium is applied once within a few days of the completion of the roentgen treatment. Filtration 2 mm. platinum. Time usually thirty hours, giving a total of 3,000 mg-hr.

They have used this technique three years. They have 5 patients well after that time. Forty are living less than three years after treatment, 30 of them more than one year, but 13 still have visible cancer. All of these patients were in Stages II and III. Of the 14 who have died all but two were in Stage III.—*Audrey G. Morgan,*

Sandler, Bernard. The radium distribution factor in carcinoma cervix therapy, with a comparison of techniques. *Brit. J. Radiol.*, Sept., 1941, *14*, 284–293.

Tables are given showing the dose delivered to different parts of the pelvis by various techniques with different methods of distribution of radium. The values assumed as maximum tolerance doses are for the vaginal vault 18,000 to 20,000 r, for the cervix 30,000 r and for the rectovaginal septum 5,000 r. An examination of the different techniques shows that if 6,000 r is accepted as the cancericidal level no technique with radium alone delivers this dosage at 5 cm. from the midline and few can deliver it at more than 3 cm. from the midline.

With all techniques it is found that the size of the vagina has a very great effect on the depth dose, an effect even greater than that of the technique used. A single source of radium will not give the best results. Radium must be applied from at least two vaginal sources. Each size of vagina must have its own technique; the vaginal tolerances must be determined and then two sources of radium used in such a way that the maximum tolerances are fully utilized; the radium must be placed as far away as possible from the vaginal mucosa and as large as possible a weight of radium must be used so that the largest possible depth dose may be given. The results showed that corks are better than box applicators.

Roentgen irradiation causes stenosis of the vagina and therefore if roentgen treatment is given some days before the insertion of radium the available space in the vagina will be reduced by the roentgen irradiation. Radium should therefore be given first or, if not, the radium should be inserted very shortly after the roentgen irradiation so that there will not be time for stenosis to occur.

Each vagina must have its own technique carefully worked out and the relations of uterine and vaginal radium to the depth dose and to each other must be determined accurately. It must be possible to give the calculated dosage exactly without any influence by the operator. Therefore factors such as different degrees of pressure in packing, the stiffness of the springs used in the Paris technique, etc., must be eliminated. A solid applicator made in sections is suggested, which fills the vagina and fornices completely so that no packing is necessary. The

distance between the radium and mucosa and between the different radium sources is exactly fixed. A specially designed applicator is necessary for each vagina in order to give the predetermined maximum tolerance dose. The radium dosage can be correlated with any roentgen technique.—*Audrey G. Morgan.*

Doub, Howard P., Pratt, Jean P., and Jones, Horace C. Combined irradiation and surgery in treatment of carcinoma of the pelvic colon. *Radiology*, Nov., 1941, *37*, 575–580.

Since 1924 the authors have used a combined method of surgery and irradiation in the treatment of cancer of the colon and rectum at the Henry Ford Hospital in Detroit. They first give roentgen irradiation consisting of a daily full erythema dose around the pelvis through four fields. The physical factors are: 200 kv., 25 ma., 50 cm., focus-skin distance, 0.5 mm. copper and 1.0 mm. aluminum filtration, 720 r. After from four to six weeks, operation is performed. The technique has to be varied according to the case but in the majority of cases a one-stage abdominoperineal or combined anterior and posterior resection can be used. Some surgeons condemn preoperative irradiation because they say it increases the risk of operation but the authors have found, on the contrary, that it decreases it. Possibly part of this difference of opinion is due to the time interval between irradiation and operation. If operation is performed too soon during the period of engorgement it may increase the risk. But if it is postponed until the patient's physical condition has reacted favorably it decreases the risk. Irradiation also seems to furnish a certain degree of protection against peritonitis. This finding has been confirmed by animal experiment.

In the authors' series of cases there was 8 per cent postoperative mortality, 46 per cent lived less than five years and 46 per cent more than five years. If the cases are counted in which only surgical excision was performed the percentage of five year survivals is 60 per cent. This is probably because the cases treated by operation alone were early cases, while many of those treated by irradiation were inoperable until after irradiation was given. This method seems to raise the limit of operability in patients who otherwise would be inoperable.—*Audrey G. Morgan.*

Bowing, Harry H., and Fricke, Robert E. Malignant disease of the rectum and rectosigmoid treated with radium. *Radiology*, Nov., 1941, *37*, 569–574.

It has been calculated that 5 per cent of all malignant disease of the body occurs in the sigmoid and rectum. If untreated, rectal cancer is very painful and accompanied by hemorrhage, foul rectal discharge and total disability. About 65 per cent of the cases are inoperable when they come for treatment. The great importance of radiation therapy is therefore apparent for life can be lengthened and made much more comfortable for these patients. They are usually elderly people with other degenerative diseases.

Treatment is generally with radium which may either be implanted in the tumor or if the tumor is accessible given by the contact method, two tubes containing approximately equal amounts of radon filtered through 0.5 mm. silver and 1 mm. brass enclosed in 2 mm. soft rubber being strapped together to form a small plaque which is placed directly against the tumor. Several applications may be necessary, probably one a day, to cover the entire growth adequately. The usual dosage for cases which have not had colostomy is from 40 to 100 mc-hr. per square centimeter of diseased surface. The total dose is heavy. A table is given showing the dosage at various depths with given amounts of surface radiation.

No routine technique can be given because the cases vary so greatly. The results depend to a great extent on the skill, care and patience of the radiologist. Treatment is necessarily difficult and tedious. Early diagnosis and treatment of polyps of the rectum should reduce the incidence of cancer of the rectum. In 1934, 500 cases were reported from the Mayo Clinic. Of this group 193 (39 per cent) survived for three years, five years or ten years or more. Counting only the patients who were given preoperative treatment 45 per cent survived.—*Audrey G. Morgan.*

Priestley, J. T., and Schulte, T. L. The treatment of Wilms' tumor. *J. Urol.*, Jan., 1942, *47*, 7–10.

The proper method of treatment of Wilms' tumor is still a subject of controversy. Most urologists agree on preoperative irradiation, nephrectomy and postoperative irradiation.

The finding of viable tumor cells at operation after preoperative irradiation indicates that irradiation alone is not adequate. At the Mayo Clinic no case of Wilms' tumor treated by irradiation alone survived for five years.

An argument which has been advanced for immediate operation without preliminary irradiation is that metastases may occur during the three to six week interval which treatment requires. This argument was felt to be applicable in one of the authors' cases in which a chest roentgenogram prior to beginning irradiation showed no evidence of metastasis. One month later, a chest roentgenogram after nephrectomy showed extensive pulmonary metastases. Obviously, it could not be proved that these metastases were not present on the original examination although not demonstrable.

Arguments in favor of preoperative irradiation are that surgical removal is facilitated due to decrease in size of the tumor. This means less operative morbidity and mortality.

In the experience of the authors the best results have been obtained from nephrectomy combined with pre- and postoperative irradiation.—*R. M. Harvey.*

Munger, A. D. Experiences in the treatment of carcinoma of the prostate with irradiation of the testicles. *J. Urol.*, Nov., 1941, *46*, 1007–1011.

The occasional beneficial results occurring in cancer of the breast following irradiation of the ovary suggests the possible value of suppression of testicular function in cancer of the prostate. Testicular hormonal activity can be suppressed by delivery of 500 roentgens to the testicle. In a series of 11 cases the author delivered 500 roentgens to each testicle by means of supervoltage therapy in addition to the scattered radiation that was delivered there from other portals used in the routine treatment of the prostate gland.

Of 45 cases treated by resection and irradiation, 10 survived while 8 of 11 cases treated with resection, irradiation and additional testicular irradiation survived. The survival time of 5 of the 8 patients ranged from three to seven years. The prostatic bed appears much more resilient in these cases as compared with similar cases treated without the additional testicular irradiation. In 2 cases with pelvic metastases, the metastatic sites appear to have become stabilized although still present.

The author feels that additional irradiation to the testicle adds something definite to the treatment of cancer of the prostate.—*R. M. Harvey.*

Randall, A. Irradiation control of testicular tumor metastases; return of renal function after long apparent absence. *J. Urol.*, Dec., 1941, *46*, 1144–1148.

Intravenous urography is of value in the study of metastasis of testicular tumors. In a study of 17 cases of testicular tumor the author has encountered 7 cases of complete unilateral anuria, indicating renal dysfunction. The diagnosis in 6 of the 7 cases was established by orchidectomy. In all cases active irradiation was employed and in 3 disappearance of the abdominal mass occurred with subsequent return of the anuric kidneys to apparently normal function. Of these 3 cases 2 are alive and all of the 4 are dead in whom renal function did not return following irradiation.

There were varied explanations for the cause of the anuria in the different cases. In the 4 cases which terminated fatally ureteral obstruction was present in 2, the kidney was invaded by the tumor in the third and the renal vein was invaded by the tumor in the fourth case.

Of the 3 cases in which return of function could be demonstrated in a previously anuric kidney, a late obstructive uropathy developed in one. In the other 2 the author suggests as the mechanism for the anuria renal ischemia secondary to lymphatic stasis. This could result from an increase in intrarenal pressure.—*R. M. Harvey.*

Mertz, H. O., Howell, R. D., and Hendricks, J. W. The limitations of irradiation of solid renal tumors in children. *J. Urol.*, Dec., 1941, *46*, 1103–1120.

Preoperative and postoperative irradiation is only an adjuvant to surgical removal in treatment of kidney tumors. Apparent clinical cures have been reported following irradiation alone. The authors employed roentgen radiation in the treatment of 11 renal tumors, in children. In 3 of these tumors the lesion proved to be cystic at operation and irradiation had no effect on the size of the tumor. Irradiation also had no effect on a polycystic kidney. In 3 patients the tumor mass became smaller but all 3 died with a palpable tumor and no autopsy was permitted.

Roentgen treatment was not complete in 2 cases. Only 3 of the group with solid renal tumors had adequate irradiation and subsequent pathological diagnoses of the irradiated tumors. All cases were treated at 50 cm. with 200 kv. and a Thoraeus filter.

The first patient was a white male, aged twenty months, who had a large embryonal adenomyosarcoma which could not be adequately irradiated due to severe gastrointestinal upsets following each attempt. The few treatments given had no effect on the tumor. The dosage given is not stated by the authors.

The second case was an embryonic adenomyosarcoma of the left kidney in a male, aged eleven years. He received 2,000 r (measured in air) to an anterior and posterior portal over the kidney with daily treatments of 200 r to one portal. This gave an estimated tumor dose of 2,960 r. Three months later, 2,000 r was given to an anterior, posterior and lateral portal with an estimated tumor dose of 4,000 r. A left retrograde pyelogram at this time showed an almost normal kidney. Treatment was continued at three month intervals for a total estimated tumor dose of 9,200 r. The mass appeared to regress following the first two courses but after the third course it began to grow rapidly and the patient died fourteen months after he was first seen.

The third case of embryonic adenocarcinoma was in a male, aged twenty-nine months. This case received an estimated tumor dose of over 16,000 r. The child has survived more than three years and is apparently clinically cured.

The authors make a plea for larger dosage in these cases, continued for an indefinite period with shorter rest periods.—*R. M. Harvey.*

Kreutzmann, H. A. R. The treatment of Hunner's ulcer with deep x-ray therapy. *J. Urol.*, Nov., 1941, *46*, 907–912.

Fulguration has proved to be the most effective method of treatment in Hunner's ulcer. The author was made aware of the value of roentgen treatment in this condition by a patient who had a Hunner's ulcer and menopausal uterine hemorrhages. Roentgen treatment of the uterine hemorrhage resulted in cure of the ulcer, which had recurred following fulguration. Five other patients in whom Hunner's ulcers recurred after other forms of treatment were subjected to deep roentgen therapy. The factors were: 200 kv. at 50 cm. tube-skin distance, with a filter of 0.5 mm. of copper and 1 mm. of aluminum. Anterior and posterior portals were used.

The usual dosage administered was 1,200–1,500 roentgens to each portal. No improvement occurred in 3 cases. In the other 3 cases complete symptomatic relief occurred together with disappearance of the ulcer for periods ranging from seven to twelve months. The author says that this compares favorably with the results from fulguration.

The dangers are possibility of producing permanent skin changes from repeated series of treatments and production of the menopause in young women.—*R. M. Harvey.*

Hauser, Harry. Roentgen therapy in tuberculous cervical lymphadenitis. *Radiology*, Sept., 1941, *37*, 304–309.

The treatment of choice in tuberculous cervical adenitis is roentgen irradiation combined with conservative surgery.

The author reports a series of 108 cases treated from 1932 to 1940. All types of the disease were treated. Eighty-seven of the cases were followed up for from a few months to seven years. Among these the results were satisfactory in 88.5 per cent and unsatisfactory in 11.5 per cent.

As this is a chronic inflammation small doses of irradiation should be given at comparatively long intervals over a long period of time. The author's technique was: 200 kv., 0.75 mm. copper plus 2.0 mm. aluminum filtration, half-value layer 0.9 mm. copper, 50 cm. target-skin distance, 150 r every ten days for 100 days or a total dosage of 1,500 r. With 20 ma. current the output was 35 r per minute. In bilateral lesions the dosage was 100 r on each side of the neck giving a total dosage of 1,000 r on each side. The field irradiated was larger than the involved area.

The prolongation of the irradiation prevented skin damage even if the series was repeated six months to a year later. However, a second or third repetition may injure the skin.

Two cases are described in detail to illustrate satisfactory and unsatisfactory results. In the second case in which the local results were unsatisfactory the patient's general condition was nevertheless greatly improved. She was a woman of forty who had had enlarged glands since she was fourteen years of age.—*Audrey G. Morgan.*

Kelly, James F., and Dowell, D. Arnold. Twelve-year review of x-ray therapy of gas gangrene. *Radiology*, Oct., 1941, *37*, 421–439.

The first report on the roentgen treatment of gas gangrene was made in 1931. Up to that time the mortality from that disease had been 50 per cent or more, and many amputations had been performed. In the group of 8 cases reported at that time the mortality was only 25 per cent with no removal of tissue after roentgen treatment had begun. Tables and graphs are given showing the mortality in the authors' own cases and cases collected from the literature since that time. In 364 cases with one or more roentgen treatments the mortality was 11.5 per cent; in 288 cases with three or more roentgen treatments 5.9 per cent, and in 42 cases with three or more roentgen treatments and no serum 4.7 per cent. So with roentgen treatment gas gangrene can no longer be considered a really serious disease.

The mortality was higher in cases treated on clinical evidence alone than in those in which laboratory examination showed *Cl. welchii*. That is, the inclusion of cases with doubtful diagnosis raised rather than lowered the mortality.

Amputation is not indicated in these cases. Only such tissue should be removed as is necessitated by the wound. No major surgery should be performed during the acute toxic stage for the infection itself. Nor should either serum or sulfonamides be used in conjunction with the roentgen treatment. The antitoxic action of roentgen therapy is evidently nonspecific and can be used in other infections, such as peritonitis and osteomyelitis.

Irradiation can also be used prophylactically. A number of cases are described in detail, showing the method of use and the results of the treatment.

In the discussion, Dr. McNamee objected to the use of the term prophylactic. He said that what was described as prophylaxis was really only very early treatment before clinical signs of the disease had developed. Dr. Kelly replied that what he had called prophylactic irradiation is not a vaccination but that it is prophylaxis in the sense that it prevents the infection from becoming established. In reply to a question in regard to dosage he said that they gave for treatment 150 r per day in two doses of 75 r or three doses of 50 r each to the entire abdomen or the area believed to be infected. For prophylaxis they give one dose of 75 r per day. From 90 to 130 kv. is used, depending on the thickness of the part and filtration is increased with kilovoltage.—*Audrey G. Morgan.*

Dowdy, Andrew H., and Sewell, Robert L. Roentgen radiation in experimental Clostridium welchii infection (gas gangrene) in dogs. *Radiology*, Oct., 1941, *37*, 440–442.

Experimental work in gas gangrene on small animals has been unsatisfactory because of the irregular and unpredictable course of the disease. But the authors have succeeded in producing an infection quite similar to that in man in dogs. They injected material from a twenty-four hour unwashed culture of gas bacilli intramuscularly into the thigh of the dogs. Sixty-six dogs were inoculated, 16 being used for biological standardization, 25 for the tests and 25 as controls. After the injections they were irradiated with an individual dose of 100 r (measured in air), portal from 20×20 cm. to 20×30 cm. Morphia was given in some cases to keep the animals quiet. The survival was 36 per cent among the irradiated animals and 20 per cent in the control group. The average survival period was almost twice as long in the irradiated as in the non-irradiated animals—45.4 hours as compared with 24.5 hours. The results are more striking when the factors of time between inoculation and irradiation, amount of treatment, dosage and kilovoltage are taken into consideration, and a table is given showing the effect of some of these factors. For instance in a group of animals given 1.25 cc. of the material (the lethal dose) or more, survival in the irradiated animals was 31 per cent and in the non-irradiated animals only 12.5 per cent. Further study is to be made of the effect of varying these factors and of the effect of using sulfanilamide compounds alone or in conjunction with irradiation.—*Audrey G. Morgan.*

Hodges, Fred M., Snead, L. O., and Berger, R. A. Roentgen therapy of hemangiomata. *Radiology*, June, 1941, *36*, 700–705.

Radium treatment has been quite generally used in the treatment of birthmarks. The authors find that equally good or better results can be obtained in certain types of these lesions by the use of roentgen rays. Filtered rays are used in certain selected cases of cavernous hemangiomata and contact therapy in the more

or less superficial strawberry birthmarks. Three illustrative cases are described, in the first of which a very large cavernous birthmark of the ear and face was reduced to only slight discoloration by treatment continued over thirty months. During this time the child was given 1,440 r filtered through 3 mm. aluminum at a focal skin distance of 25 cm. and at 135 kv. She was never given more than 200 r delivered in air at one treatment, more often 120 r at the rate of 40 r per minute. Contact therapy is now being used to overcome the remaining discoloration. Among 19 infants treated for strawberry birthmarks by the contact therapy method 9 have been discharged with so little discoloration that the lesion could not be located if its presence was not previously known. Of the remaining patients none has been under observation more than six months.

With contact therapy they give one treatment in four to six weeks. The dose is only of three seconds' duration, during which 400 r in air is delivered. This produces little or no reaction in the tenderest skin of the youngest infant.—*Audrey G. Morgan.*

Arons, Isidore. Further studies on radiotherapy of lymphoblastoma. *Radiology*, Aug., 1941, *37*, 164–173.

In the course of the past ten years the author has treated 45 cases of lymphoblastoma, consisting of 12 cases of Hodgkin's disease, 15 of lymphosarcoma, 13 of leukemia and 5 on the borderline between leukemia and lymphosarcoma. Eight of the cases are described and illustrated with roentgenograms and the details of the roentgen treatment given in the case histories.

It has been found that normal function of the reticulo-endothelial system is a major factor in resistance to malignancy. This is particularly true in malignant disease of the lymphatic system. Therefore modern treatment of the lymphoblastomas aims to give a dosage sufficient to destroy the local lesions without injuring the reticulo-endothelial system. The massive doses that were at first given with disastrous results are no longer used. The low voltages formerly used have been increased to the present high voltages. The doses are now fractioned, the doses being given at brief enough intervals to ensure continuous radioactivity and to prevent the recovery of malignant cells not completely destroyed.

As autopsies have shown that the areas of malignant proliferation are larger than shown clinically, extensive irradiation should be used. The author thinks, however, that irradiation of the whole body should be used only in selected cases. Irradiation of the spleen—small doses over three fields—is of value in some cases of lymphoblastoma.

Experimental work has shown that involvement of the spleen is accompanied by a high percentage of involvement of the lungs.

Irradiation with small doses and short intervals is only palliative but may treble the life expectancy of the patient.—*Audrey G. Morgan.*

Popp, Walter C., and Watkins, Charles H. Roentgen therapy for chronic macrolymphocytic and mesolymphocytic lymphatic leukemia. *Radiology*, Aug., 1941, *37*, 160–163.

The authors describe what they consider a special phase of lymphatic leukemia rather than a new type of the disease. It is characterized by the fact that a large majority of the lymphocytes are of the macrolymphocytic or mesolymphatic type. At first glance the picture might be confused with that of acute leukemia but a close examination of the cells shows that they are not lymphoblasts.

Special care is necessary in the roentgen treatment of this phase of the disease as these cells are particularly sensitive to irradiation. Also irradiation with large doses is apt to bring about a rapid increase in blood urea, either from difficulty in eliminating the waste products of the destruction of leukocytes or from involvement of the kidney itself. Too great reduction of the number of leukocytes should also be avoided. When the count is around 75,000 reduction to 25,000 to 30,000 is sufficient and proportionate reduction with other counts.

They give not more than 100 to 125 r per field with about 130 kv. Only one treatment is given per day and they are continued daily until the count has reached the desired level. Frequent leukocyte counts and blood urea determinations should be made.

Dr. Haden said be believed the disease described was more closely related to sarcoma than the classic lymphoid leukemia. Such cells are sensitive to irradiation. Dr. Portmann said he believed he had not made a special classification of the type of leukemia described. He has, however, given roentgen treatment to patients in the leukopenic stage of leukemia with good

results. In these cases he gives spray irradiation anteriorly and posteriorly in small doses—25 to 50 r—on alternate days. He has had bad results in only 1 case in which an overdosage was given. Dr. Newell said he believed in giving the smallest dosage that gives results in all cases of leukemia. He generally starts with a dosage of 25 r rather than 100 r. He does not understand the authors' fear of a low white count. Even if the count goes down to 6,000 it is not alarming if this fall has been brought about by small doses of irradiation. Dr. Popp in closing said there is probably no disease in which there is greater confusion in classification than in leukemia. He believes the type described by him and his colleagues is a distinct entity and should not be confused with leukosarcoma.—*Audrey G. Morgan.*

Jacox, Harold W., and Freedman, Lester J. The roentgen treatment of myxomatous cutaneous cysts. *Radiology*, June, 1941, *36*, 695–699.

The authors describe 7 cases of myxomatous skin cysts seen at the Western Pennsylvania Hospital in the course of three years. This incidence in an active dermatological service shows that these cysts are not very frequent. They were formerly confused with synovial lesions of the skin but the differentiation should be made as surgery is effective in the latter while the myxomatous cysts are apt to recur after surgical removal.

These cysts are caused by degenerative changes in the corium, the etiology of which is not known. They are not reducible by pressure as the synovial cysts are and as they are a part of the corium the skin cannot be moved over them. They are best treated by low voltage roentgen therapy, 100 kv. constant potential, 4 ma., 30 cm. focal skin distance, no added filtration, 120 r per minute, 1,400 to 1,600 r at one treatment. The field should be limited to the base of the lesion and the surrounding skin adequately protected. The doses formerly used were too small to be effective.—*Audrey G. Morgan.*

Cipollaro, Anthony C. Irradiation in dermatology. *Radiology*, June, 1941, *36*, 684–694.

There is a great lack of uniformity in the technique of irradiation in skin diseases. In general, roentgenologists tend to use higher voltages, greater filtration, larger doses and shorter intervals between treatments while dermatologists use lower voltages, little or no filtration and smaller doses with longer intervals. Certainly the quality of rays should be used which gives the best results with the least damage to underlying structures. A chart is given which shows absorption curves with depth doses of various radiations used in dermatological practice superimposed, with correct dimensions, over a cross-sectional diagram of the skin. The peak voltages varied from 40 to 140 kv. It shows that for routined ermatologic treatment unfiltered roentgen rays generated with 40 kv. are as effective as those generated with 100 kv. Certainly 100 kv. rays are more than adequate to reach pathological lesions in the skin. In support of his thesis that high voltage heavily filtered rays are unnecessary and even undesirable in dermatologic practice the author discusses the treatment of a number of the commoner skin diseases.

In the discussion Dr. Driver said that the less irradiation given consistent with good results the better. Nor should irradiation be repeated too often for such diseases as acne vulgaris, particularly in young people less than seventeen or eighteen years of age. The need of a complete knowledge of the treatment used was also emphasized.—*Audrey G. Morgan.*

Ashbury, Howard Hicks. An ointment for the relief of discomfort due to severe irradiation epidermitis. *Radiology*, June, 1941, *36*, 739.

In the ordinary skin reaction caused by irradiation the discomfort can be controlled by aquaphor. But the author describes a case of severe reaction from irradiation of cancer of the vulva. This is a particularly sensitive area and the skin and mucous membrane were completely denuded. Relief was obtained by the local application two or three times within twenty-four hours of an ointment made by the addition of 0.5 to 1 per cent of tetracaine to the aquaphor.—*Audrey G. Morgan.*

Roberts, Ff. The limitations of biopsy in x-ray therapy. *Brit. J. Radiol.*, April, 1941, *14*, 144–145.

There has been an increasing tendency on the part of radiologists to demand biopsy examinations before giving treatment. The author believes that this tendency has been exaggerated

and that, if there are clinical and roentgenological evidences of malignancy, treatment should be given without waiting for a pathological examination. In the first place, the patient is apt to be very sick and should not be subjected to additional unnecessary strain. Then there is the possibility that a malignant growth may be disseminated. Biopsy often does not give a definite result; the part of the growth that is removed may be non-malignant but there may be malignancy in other parts. The course of the treatment cannot be influenced by the finer degrees of microscopic malignancy.

Some radiologists evidently fear that if histological diagnosis is not made and a cure results discredit will be cast on their treatment on the ground that the diagnosis was incorrect. But the fact that malignant growths can be cured by irradiation has been sufficiently proved so that histological evidence is not necessary in every case.—*Audrey G. Morgan.*

Jacoby, Paul, and Spotoft, J. Investigations into the significance of the sedimentation reaction as regards the prognosis of irradiation of cancer patients. *Radiology*, May, 1941, *36*, 617–620.

This report is from the Radium Center of the Danish Society for the Campaign against Cancer in Odense, Denmark. This country is so small that it is much easier to follow up cancer patients than in larger countries. The author reports 59 cases of cancer of the breast and 39 with cancer of the uterus in which sedimentation tests were made before treatment and afterwards at varying intervals. Tables are given showing the details of the results.

The prognostic significance of the sedimentation reaction cannot be judged until about a year after the beginning of treatment. The figures for both groups of cases show that increased sedimentation reaction has an unfavorable prognostic significance. The use of the sedimentation reaction in the control of cancer patients should be continued.—*Audrey G. Morgan.*

MISCELLANEOUS

Lindgren, Erik. An apparatus for radiography in immediate connection with radioscopy. *Acta radiol.*, 1941, *22*, 383–386.

The author describes and illustrates an apparatus for taking roentgenograms in immediate connection with screen examination of the duodenum. In this way no changes take place in the condition of the organ between the time of the fluoroscopic examination and the making of the permanent record. It is so arranged that it can be switched from the screening side to the exposure side by the nurse at a given signal from the doctor. Many similar devices have been used before but the author thinks his is simpler, lighter and less expensive than most of those in use heretofore.—*Audrey G. Morgan.*

Clark, K. C., and Poulsson, K. T. Further experiments in x-ray screen photography (1011 subjects with control direct radiographs). *Brit. J. Radiol.*, July, 1941, *14*, 250–254.

Miniature screen photography and comparative direct roentgenography was carried out in 1,011 cases, 771 of the subjects being Norwegian seamen escaped from the Lofoten Islands in March, 1941; they were of outstanding physique. The others were students, office workers, factory hands, etc. The details of the screen photography are discussed and a table given showing the findings in the 55 cases in which there were pathological conditions.

Two physicians examined the miniatures and control direct roentgenograms. The less experienced of these found 11 discrepancies and the more experienced 10. The discrepancies found were of no clinical significance. Evidently if first-class technique is used screen photography very closely approximates if it does not equal the results of the usual direct method in distinguishing the normal from the pathological. Definite active tuberculous lesions were found in 13 of the cases, including 2 of pleural effusion. None of these lesions were overlooked in the miniatures.—*Audrey G. Morgan.*

Hodes, Philip J., and Griffith, John Q. Effect of roentgen irradiation upon lymphatic flow in rats. *Radiology*, Aug., 1941, *37*, 203–204.

Rats were irradiated to determine whether roentgen irradiation has any effect on the flow of lymph. Two groups were treated—one with 135 kv., 4 ma., 0.25 mm. copper plus 1 mm. aluminum filtration, 30 cm. target-skin distance, total dose to skin 2,250 r (in air) given at one time in about forty minutes. Twenty-one to twenty-five days later thorotrast was injected into the dorsum of each foot. One hind leg of each rat had been irradiated while the other was used as a control. The other group was treated

with 200 kv., 20 ma., 0.75 mm. copper plus 2.0 aluminum filter, 25 cm. target-skin distance, total dose 2,200 r in air delivered at one time in about twenty minutes. Injections of thorotrast six weeks after irradiation.

In neither group was there any appreciable interference with the flow of lymph. But much more experimentation is necessary before these results can be applied to human problems. Different daily doses and a much wider range of time interval after irradiation must be used. Possibly colloid dye studies would be more effective in determining the rate of lymph flow.—*Audrey G. Morgan.*

Glücksmann, A. Preliminary observations on the quantitative examination of human biopsy material taken from irradiated carcinomata. *Brit. J. Radiol.*, June, 1941, *14*, 187–198.

The biological response of both normal and malignant cells to radiation has been studied quantitatively at the Strangeways Research Laboratory, Cambridge. In this paper a method is described by which the effects of radiation on living malignant cells in biopsy material is measured quantitatively. The method so far has been applied only to the primary growth in squamous and basal cell carcinomata. Biopsies were taken before treatment and at different intervals during and after treatment. They were cut at right angles to the surface of the tumor so as to include the growing edge and both malignant and normal tissue.

All the cells in selected young areas of tumor growth were counted and divided into four classes: dividing, degenerate, resting, and differentiating cells. Graphs are given showing the percentages of these different types of cells at various times during and after the treatment. The resultant curves can be used somewhat as blood counts are used in blood diseases for determining the response of the tumor to treatment. The effectiveness of the treatment can be judged by the quantitative differences in the different types of cells in counts made at the different periods. The method is to be tested on a larger scale.—*Audrey G. Morgan.*

Sugiura, Kanematsu. The effect of high and low body temperatures upon the growth of irradiated mouse sarcoma 180. *Radiology*, July, 1941, *37*, 85–93.

The author believed that the growth of mouse tumor might be affected by the body temperature of the animals. The experiments which he performed in the attempt to settle this question are described in detail and illustrated. Fever was brought about by the use of short and ultra-short radio waves, cold by keeping the animals in the refrigerator. Mouse sarcoma 180 was used for the experiments.

When animals with tumors were irradiated with 200 kv. and then subjected to ultra-short radio waves until the rectal temperature was 40° to 43° C. the number of tumor regressions was definitely increased. With doses of 1,000 r the regressions increased from 50 to 75 per cent.

When the temperature at which the irradiated mice was kept was reduced to −10° C. the animals all died within a few hours. When they were kept at temperatures of 3° to 5° C. they survived but the number of tumor regressions was decreased. With a dose of 100 r the decrease was from 50 per cent to 27 per cent.

A study was also made of the resistance of mouse sarcoma 180 to cold in vitro. Bits of tumor tissue were kept at −70° C. for varying periods and then inoculated into normal mice. The capacity of the tumors for growth was only slightly inhibited by this procedure. The growth of the tumors was greatly delayed for the first week but after that it was normal. It made no difference whether the tumor fragments were kept for one hour or for seven days in the frozen state. The injurious action of the cold on the tumor cells was due to the initial rapid freezing and not to keeping them frozen for long periods. —*Audrey G. Morgan.*

Denstad, Torfinn. Die Strahlensensibilität des Knochenmarks. (The radiosensitiveness of the bone marrow.) *Acta radiol.*, 1941, *22*, 347–359.

The animal experimentation which has been done on the effect of irradiation on the blood has not given uniform results and besides the findings cannot be applied to human pathology. The author has therefore studied the action of irradiation, both radium and roentgen, on the bone marrow in human subjects being treated for cancer. The roentgen treatment as a rule was given with hard rays—175 kv., 4 ma., 2 mm. copper and 3.5 mm. aluminum filter, 60 cm. distance. Material for examination was obtained by puncture of the sternum.

It was found that the red marrow is very sensitive to irradiation. Marked changes took place even after the small doses used in the treatment

of inflammation and arthrodesis. Both the erythropoietic and the myopoietic cells were affected, the most immature cells being the ones that disappeared quickest. The bone marrow showed a very great capacity for regeneration. Even with the largest therapeutic doses there was almost complete anatomical regeneration after one to a few months. But the blood changes were more persistent. A marked leukopenia, chiefly lymphopenia, sometimes persisted for a year after treatment, though the general health was not affected. This leukopenia is doubtless due to the inhibiting action of the irradiation on myelopoiesis and lymphopoiesis. This inhibition is evidently due to a distant action of the rays and occurs whether the marrow is irradiated directly or not. Total irradiation is probably the best palliative treatment for leukemia.—*Audrey G. Morgan.*

Fried, Carl. The roentgen treatment of experimental pneumonia in the guinea-pig. *Radiology*, Aug., 1941, *37*, 197–202.

It has been found empirically that roentgen irradiation in pneumonia brings about decline of the fever, disappearance of dyspnea, general improvement and shortening of the course of the disease.

The author experimented on the irradiation of artificial pneumonia in guinea pigs in an attempt to account for this improvement and to determine whether it could be counted on in all cases. The animals were infected by giving them an intratracheal injection of an emulsion of *Staphylococcus aureus haemolyticus*. Less than lethal doses were given so that the controls could be used for purposes of comparison. The irradiated animals showed the same clinical improvement as human subjects. Macroscopically the lungs of the non-irradiated animals showed hepatization while those of the irradiated animals were soft and normal in color and consistency. Histological examination showed infiltration in the non-irradiated animals and normal alveoli in the irradiated ones. Obviously irradiation hinders the development of pneumonia and the earlier it is given after infection the better the results.

The course of the experimental pneumonia in animals is fundamentally the same as that of postoperative pneumonia in man and the author concludes that the results of irradiation seen in human cases have not been due to chance but to the power of irradiation to limit inflammation and influence the mechanism of healing.—*Audrey G. Morgan.*

Chambers, Robert, and Cameron, Gladys. The reaction of kidney tubules in tissue culture to roentgen rays. *Radiology*, Aug., 1941, *37*, 186–193.

These experiments were made with a view to determining whether cells when physiologically active are more susceptible to the action of roentgen rays than when they are not. The tissue used was from the mesonephros of nine or ten day chick embryos grown in tissue culture. Experiment has shown that these tubules continue to function in tissue cultures. The outgrowth from the explant consists of wandering cells, fibroblasts and sheets of proliferating epithelium so that the cultures provide a method of studying epithelial tissue as organized tissue in the form of secreting tubules and as unorganized tissue in the form of outgrowing sheets.

It was found that organized secreting tubules and wandering cells were far more sensitive to the action of the rays than unorganized epithelial sheets. The distal tubules were found to be more radioresistant than the proximal tubules.

Doses of 5,000 to 75,000 r were used. Large doses of 25,000 r were required to bring about definite effects within several days.

The results of the experiments show that cellular activity is a factor in increasing the susceptibility of cells to the destructive action of irradiation. The susceptibility of the tubules was increased when their secretory activity was stimulated by the addition of phenol red or magnesium sulphate to the medium.

The renal cells are capable of recovering from the effects of sublethal doses of irradiation, as shown by the fact that if they are stimulated to secrete soon after irradiation they die, but if time is allowed for them to recuperate they can do the extra work required by the stimulation without deteriorating.—*Audrey G. Morgan.*

Henshaw, Paul S. The induction of multipolar cell division with x-rays and its possible significance. *Radiology*, June, 1941, *36*, 717–724.

There is apparently a paradox in the fact that irradiation causes cell death and yet may also cause the unrestrained growth of cancer.

When fertilization takes place the fertilized egg practically always divides into two equal blastomeres but if either of the gametes is ir-

radiated before fertilization takes place cleavage takes place not into two blastomeres but into several. This multipolar cell division usually causes early death of the cell progeny. There is as yet no record of multipolar division actually having caused tumor but it seems possible that it may cause changes in hereditary substances which make malignant growth possible. Experimental work has shown some interesting facts bearing on this problem. If young mice from a high-breast-cancer strain are foster-nursed by mother from a low-cancer strain few cancers will develop among them, but if the young of low-cancer strains are nursed by mothers of high-cancer strains there will be many cancers. This indicates that there are two factors in the causation of cancer—one in the hereditary background and one in the milk. Possibly radiation acts as the stimulating factor that rouses into activity certain hereditary factors capable of causing malignancy.—*Audrey G. Morgan.*

Westermark, Nils. A study of the cardiac movements simultaneously recorded by roentgen-cinematography and electrocardiography. *Acta radiol.*, 1941, *22*, 393–403.

The author describes experiments made on sheep which show how complicated the movement of the heart is, not only during the active phase of systole but also during the passive phase of diastole. Five metallic indicators were inserted into the wall of the left ventricle and roentgen cinematography and electrocardiography carried out at the same time. By the method used, which is described, the records of the two methods of examination could be compared with an accuracy of 1/18 to 1/24 second. Diagrams are given of the position of the indicators in the wall of the ventricle and graphs show the paths of the indicators during the revolution of the heart.

They show that the anterior part of the base of the ventricle makes a piston-like movement with the downward phase at the beginning of diastole and the upward movement during the end of systole. The anterior part of the base of the ventricle remains perfectly quiet during diastole. Apparently, therefore, a contraction of the rest of the wall of the ventricle has taken place during systole. Except for a tendency of the wall of the ventricle to approach the base of the heart, no contractile movement of this kind could be demonstrated definitely on the outlines of the wall of the ventricle. These outlines seemed to describe a pendulum-like and rotatory movement caused by the movements of the whole heart.—*Audrey G. Morgan.*

Taylor, Lauriston S. New x-ray laboratory of the National Bureau of Standards. *Radiology*, July, 1941, *37*, 79–84.

During the past ten years the voltage of roentgen treatment apparatus has been increased from 200 kv. to about 1,000 kv. The problem of the establishment of suitable standards for such voltages has been turned over to the Bureau of Standards and a laboratory has been built for this purpose at a cost of about half a million dollars. This laboratory and its equipment is described in detail and a floor plan of the first floor and roentgen-ray laboratory given. The space is divided about equally between the roentgen-ray section and the high-voltage measurements section. The building is five stories in height. At the time this article was written the installation of the 1,000 kv. equipment had been completed and the equipment was in operation. The 400 kv. equipment on the second floor had just been completed and standardization work was to be begun.—*Audrey G. Morgan.*

Cassen, Benedict. Some recent contributions of physics and engineering research to radiology. *Radiology*, Sept., 1941, *37*, 338–342.

The author pays tribute to the great value of the work of physicists and engineers in the progress of radiology. He discusses a number of recent contributions, among them ignition timing, air cooling for therapy tubes, the polarized stereoscope, which makes it possible for a number of observers to obtain stereoscopic vision of roentgenograms at the same time, and the substitution for the old feathered copper-glass seals of Kovar-glass seals. The technical details of these discoveries are described and illustrated with diagrammatic drawings. They are all contributions to roentgenography except the air cooling of therapy tubes which is of value in treatment.—*Audrey G. Morgan.*

Stanford, Brian. A research into the physical factors concerned in indirect radiography. I. The optimum combination of film and fluorescing screen for use in indirect radiography. *Brit. J. Radiol.*, April, 1941, *14*, 128–135.

Indirect roentgenography, or the photo-

graphing of the image made on the fluoroscopic screen, has not been very widely used practically in England. The author therefore proposes to consider in a series of papers the various physical factors involved in the process. In this paper he considers the effect on density of the image of different combinations of photographic emulsion and fluorescing screen. Eleven emulsions and five screens were tested in all possible combinations with regard to their effect on density, the other factors being kept constant. The technique of the experiments is described and tables given showing the details of the results. One table shows the results obtained for the three most effective screens and various emulsions that can be obtained commercially.

Of course under a different set of conditions with regard to the roentgen-ray beam these findings might be changed.—*Audrey G. Morgan.*

Stanford, Brian, A research into the physical factors concerned in indirect radiography. III. A simple method of detecting experimentally the presence of the phenomenon of latent image reinforcement in a fluorescing screen. *Brit. J. Radiol.*, June, 1941, *14*, 213–214.

With some fluorescing screens a subject previously recorded may reappear when the screen is used again, appearing as a ghost image that confuses the clarity of the second image. This is permissible to some extent in recording screens as the phenomenon persists for only a short time and they are rarely used twice at such short intervals. But in mass roentgenography the image on the screen may be changed every few seconds and so such reinforcement is not permissible.

A simple method of testing a screen for this phenomenon is described. Exposure is made on the screen of a steep roentgen-ray step-wedge, which is then rotated for 90° and a second exposure made. If there is no latent image reinforcement, only the second image will appear on the screen. Screen G 231 was tested in this way and found free of the phenomenon.—*Audrey G. Morgan.*

Stanford, Brian. A research into the physical factors concerned in indirect radiography. IV. The quantitative estimation of the actinic value of the afterglow of a fluorescing screen. *Brit. J. Radiol.*, July, 1941, *14*, 244–246.

The details of an experiment performed to make a quantitative determination of the actinic value of the afterglow of a fluorescing screen are described. A G 231 200-mesh screen was used. The screen was activated regularly every ten seconds for a tenth of a second at 80 kv., 100 ma., 2 ft., 3 in. tube-screen distance. Under these conditions the useful actinic emission becomes negligible about two seconds after activation is discontinued. If a screen is used that has an afterglow a simple shutter should be used in the camera. If the viewing screen has no detectable visual afterglow it may be assumed to have no actinic afterglow and in that case a shutter is not necessary.—*Audrey G. Morgan.*

Stanford, Brian. A research into the physical factors concerned in indirect radiography. V. The effect on luminous output of variation of crystal size of the fluorescing material. *Brit. J. Radiol.*, Sept., 1941, *14*, 304–306.

The fluorescence of fluorescent screens is often accompanied by phosphorescence in which the emission of luminous energy persists after the exciting radiation has stopped. This is very undesirable as in viewing screens it leaves the trace of moving organs on the screen and blurs the image. On recording screens the imprints of former exposures are left superimposed on more recent ones.

This article describes tests made to see to what extent variations of the mesh size, that is the size of the crystals constituting the salt coating, would affect the intensity of the light emitted by the screen. Five screens were tested which were specially prepared from two salt mixtures; three from salt G 231 passed through sieves of 120, 200 and 220 mesh and two from salt Y-S passed through sieves of 120 and 200 mesh. The variations in mesh size had no effect on the luminosity of salt Y-S. Mesh 200 was optimum for salt G 231, while 220 was about 10 per cent slower than this and 120 about 30 per cent slower. Increased kilovoltage resulted in proportional increase in luminosity on both screens to an equal degree throughout the range tested. The fluorazure salt, ordinarily used as a recording screen, shows an optimum response at 65 kilovolts.—*Audrey G. Morgan.*

Williams, Marvin M. D. The effect of shockproof cables and condensers on two-valve half-wave rectification. *Radiology*, July, 1941, *37*, 94–101.

Changes in the equipment for roentgen therapy in the past few years have given an opportunity to compare the quantity and quality of radiation produced by several types of rectifying circuits and particularly for determining the effect of shock-proof cables and condensers on two-valve half-wave rectification.

A series of oscillographic tracings is given for different milliamperes at several peak voltages, showing the effect of the capacity of shockproof cables and condensers on the voltage waveform from a two-valve half-wave rectifier. These different voltage wave forms cause changes in the intensity and quality of the radiation. A change of more than 100 per cent in the number of roentgens per minute per milliampere, as well as changes in the quality of the radiation may be brought about by shockproof cables, the presence or absence of other condensers and different tube currents.—*Audrey G. Morgan.*

Jacobs, Lewis G. The accuracy of focal spot size determination: some theoretical and practical considerations. *Radiology*, Aug., 1941, *37*, 214–220.

The author gives mathematical formulae for estimating the effective projected focal spot distance for clinical use without further correction, provided the tube is centered between two pinholes with its principal axis perpendicular to the line connecting the pinholes and provided the target-pinhole distance is large both absolutely and in proportion to the distance between the pinholes. As the measurement of the shadows on the film is subject to quite a large error it is best to use the average of at least ten different measurements for the values both of shadow size and of the distance between the shadows. The method is not accurate to more than 5 per cent though it is possible that its accuracy might be improved by special camera construction, especially if extra fine grain film and extremely small pinholes were used to decrease the penumbra.—*Audrey G. Morgan.*

Glasser, Otto. The evolution of dosimeters in roentgen ray therapy. *Radiology*, Aug., 1941, *37*, 221–227.

The older methods of roentgen dosimetry are described. In 1925 a Committee on Standardization of Measurement of Radiation was formed by the Radiological Society of North America. It was made up of radiologists and physicists as the importance of collaboration between these two groups was realized.

Roentgenologists are interested primarily in the average quality of the roentgen-ray beam used in treatment and its distribution in the tissues. Therefore they prefer some way of specifying quality according to absorption values. Total absorption curves in any absorbing medium can be made easily with modern ionization dosimeters, and those of constant potential apparatus have a close relationship to the spectral distribution of the radiation. Taylor in 1938 developed standard absorption curves to be used as practical "qualimeters." Absorption coefficients, effective wave lengths, average wave lengths and half-value layers can be derived easily from such absorption measurements. The preferred way of expressing quality is according to half-value layer.—*Audrey G. Morgan.*

Meyer, William H. Depth dose calculation wherein absorption in unit volume in the depth, i.e., volume depth dose, is the index of effective radiation. *Radiology*, Oct., 1941, *37*, 476–486.

The author maintains that the r dose, usually taken as the unit of dosage, varies with the voltage or filtration used, with the size of the field, the focal distance and the r per minute of application of the dose. The important thing is to bring about maximum absorption at the site of the lesion. He presents the scale of a depth dosimeter that he has worked out on the basis of many years' experience in the use of radiation therapy. It allows for the variable factors and permits of a rapid determination of depth dosage.—*Audrey G. Morgan*

Lamerton, L. F. Physical investigations with 140 kVp radiation. *Brit. J. radiol.*, June, 1941, *14*, 199–205.

Physical examinations have been made of low voltage radiation, up to 60 kv. and in the higher ranges from 180 kv. up. But very little work has been done on the intermediate range which is known as that of middle distance therapy. The author describes measurements made at 140 kv. (peak) using a Victor middle distance set. Absorption measurements were made in copper, using a Victoreen condenser dosimeter. The tube filters used were 0.25 mm. copper and 0.10 mm. copper. The half-value layers and equivalent wave lengths with these filters are

given and the absorption curve shown. Measurements of the variation of depth dose with variations in filtration showed that 0.25 mm. copper was a good filter for use in treatment. The variation of percentage backscatter with variations in the size of field was measured. Central axis depth dose curves for different field sizes and with focus-skin distances of 15.5, 20 and 25 cm. are given, as well as some complete isodose curves. Measurements of the stray radiation near the tube are also described.—*Audrey G. Morgan.*

Reinhard, M. C., and Goltz, H. L. Note on the distribution of surface radiation from a million-volt generator. *Radiology*, Sept., 1941, *37*, 335–337.

The million-volt roentgen-ray generator of the type installed at the State Institute for the Study of Malignant Disease at Buffalo in June, 1940, has two beams, one transmitted and one reflected. The target is placed at an angle of 45° to the long axis of the tube which results in a differential filtration of the radiation of the transmitted beam, with a consequent asymmetry of intensity. This asymmetry can be corrected by the introduction of wedge-shaped filters of copper or lead. These are simple and easily made and can be changed if necessary.—*Audrey G. Morgan.*

Flint, H. T., and Wilson, C. W. The homogeneity of dosage distribution in radiation teletherapy. *Brit. J. Radiol.*, Sept., 1941, *14*, 300–303.

In securing homogeneity of irradiation in the treatment of tumors with radium the method should be to provide some form of framework with the irradiation portals and central directions indicated. The field within the framework is then known and the patient must be placed so that the lesion lies in the most suitable part of the field. The principle is to place the patient within the field, not to form the field within the patient.

Such a framework or jig, designed for the treatment of tumors of the larynx is illustrated and a diagram given of the distribution of radiation resulting from three teleradium fields fixed to the jig. This arrangement provides for homogeneity of distribution of the radiation and ensures that all the diseased tissue is given adequate treatment.—*Audrey G. Morgan.*

Clarkson, J. R. A note on depth doses in fields of irregular shape. *Brit. J. Radiol.*, Aug., 1941, *14*, 265–268.

Depth doses have been worked out quite accurately for circular or square fields. But occasionally very irregularly shaped fields are used in treatment. A method of calculation is given for percentage dose rates at any point within a volume of tissue which is irradiated from a beam of roentgen or radium rays, no matter what the shape of the field. Results of the calculation of central axis depth doses for rectangular fields are also given. Tables and graphs show the details of the results.—*Audrey G. Morgan.*

Mayneord, W. V., and Lamerton, L. F. A survey of depth dose data. *Brit. J. Radiol.*, Aug., 1941, *14*, 255–264.

In working out the depth dose tables that are given at the end of this article, the authors surveyed the results of a number of other workers. These are apt to be more reliable than individual measurements made with inadequate apparatus. They concluded that sufficiently accurate tables could be drawn up not only for the 200 kv. region but also for the higher regions up to 1 million volts. The mathematical equations used in working out their results are given and the graphs showing the details of the results. The three most important factors considered were the focal-skin distance, the quality of the radiation and the area of the field. The tables give the percentage depth dose for qualities of radiation from 1.0 to 5.0 mm. copper half-value layer at depths up to 20 cm. for fields up to 400 sq. cm. in area and with focal-skin distances from 40 to 100 cm. A less comprehensive study has been made of radiation up to 17 mm. copper half-value layer and the results are shown in curves and tables. The mean values of percentage surface backscatter have been determined from the literature for fields up to 400 sq. cm. in area and for qualities up to 14 mm. copper half-value layer. A discussion is also given of the variations in half-value layer with variations in conditions of radiation.—*Audrey G. Morgan.*

Happey, F. The integration of radiation dosage and the absorption of energy in tissue for X and gamma radiation. *Brit. J. Radiol.*, July, 1941, *14*, 235–241.

At the Sheffield Radium Center the general plan is to give a uniform tumor dose of between

4,000 and 6,000 r. In deep-seated lesions a multiple field technique must be used to accomplish this and as a result much radiation is absorbed not by the tumor but by the normal tissues. The determination of this absorption is of great clinical importance. The methods of calculation for determining it at the Sheffield Radium Institute are given as well as curves and tables showing the details of the results. The calculations are made for 200 kv. radiation with a filter of 1 mm. copper and 1 mm. aluminum and fractional integrated dosage curves are given for these conditions. Corrections must be made for fields larger than 150 sq. cm.

The graphs given presuppose that all radiation is absorbed and the formulae given are not applicable to glancing fields, for which adjustments must be made.—*Audrey G. Morgan.*

Ting, T. P. A simple calculator for roentgenographic mensuration. *Radiology*, Aug., 1941, *37*, 208–213.

The author from the Department of Radiology, Peiping Union Medical College, reports a calculator for measuring the size of head or pelvis that is simple, accurate and inexpensive. It determines the object size (X) when the target-film distance (H), the object-film distance (L) and the size of the image (a) are known. The calculator is essentially a chart consisting of two superimposed plots; one is rectangular, dealing with the relationship of the target-film distance H and the object-film distance L, while the other is a polar graph of the object size, X, on a family of circular arcs indicating the various sizes of the image a. Actually the circular plot is replaced by a movable radial member which is pivoted on one end to the polar origin. A half-size reproduction of the chart is given. The mathematical formulae used in constructing the chart are also given.

To use it, first find the point where the target-film distance used intersects the object-film distance measured. Swing the radial member which is pivoted on one end to the origin, until its lower edge coincides with the point of intersection. Then on this radial member mark a point corresponding to the size of the image measured. Finally, by noting the curve on the chart which meets this point on the radial member and tracing it downward until it intercepts the horizontal axis the size of the object is obtained from the appended table. The table also gives the volume of a sphere corresponding to given measurements of diameter or circumference.—*Audrey G. Morgan.*

Marinelli, L. D. Milliammeters at ground potential in x-ray tube circuits. *Radiology*, Sept., 1941, *37*, 331–334.

In modern roentgen-ray equipment the milliammeter is usually at ground potential. But this has been brought about in two old roentgen-ray machines without making any expensive modifications. The two types of machine and the methods used to bring about the desired change are described and illustrated with diagrammatic drawings.—*Audrey G. Morgan.*